

CONCENTRATION POLARIZATION IN ULTRAFILTRATION OF MICROMODULES

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1975

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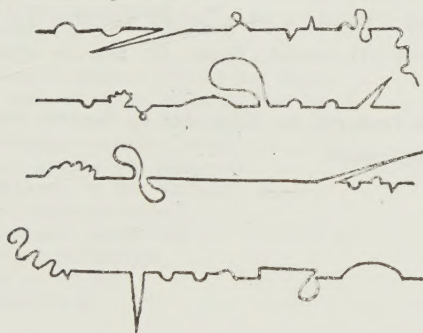


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BIBL.

In foreword to a thesis it is usual to describe one's plan of research - either the one formulated in advance or the retrospective one - and show how purposefully one has proceeded along it.

I found a good description of my course in Laurence Sterne's "The life and opinions of Tristram Shandy, gentleman".

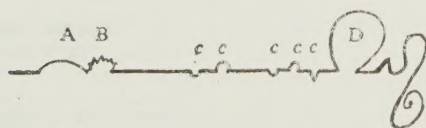
I AM now beginning to get fairly into my work; and by the help of a vegetable diet, with a few of the cold seeds, I make no doubt but I shall be able to go on . . . in a tolerable straight line. Now,



Inv. T.S.

Scd. T.S.

These were the four lines I moved in through my first, second, third, and fourth volumes.—In the fifth volume I have been very good,—the precise line I have described in it being this:



If I mend at this rate, it is not impossible—by the good leave of his grace of Benevento's devils—but I may arrive hereafter at the excellency of going on even thus:

which is a line drawn as straight as I could draw it, by a writing-master's ruler (borrowed for that purpose), turning neither to the right hand nor to the left.

I wish to thank professor B. Hallström, for creating a working atmosphere such, that I intensely enjoyed every single turn of that twisting path. I am indebted to him, to Dr. A. Klima, who introduced me to the field, and to civ.ing. P. Eriksson and Dr. J. Stocking for the critical discussions and for all the slips of pen and mind which did not appear in this thesis.

Miss A. Nykänen, Miss B. Hedlund and Mrs M. Johansson performed most of the experiments. Mrs K. Tillman typed the manuscript. Mr G. Ritzing constructed the electronics and was ever ready to help, regardless of time of day and day of week. My wife bore a double burden and my daughter did not see me as much as we all wished. Thanks for bearing with me.

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1. INTRODUCTION.

1.1. Reverse osmosis and ultrafiltration.

During the last decennium, reverse osmosis (hyperfiltration) and ultrafiltration - two techniques for separation of homogenous liquid solutions have been added to the repertoire of engineers. The terms are often used interchangeably, not only by the lay public but by some of the experts in the field as well. Others distinguish between ultrafiltration and reverse osmosis on the basis of molecular mass of the separated solutes (Madsen, 1974), applied pressure, or the mechanism of separation (Sourirajan and Matsuura 1973). In macroscopic description, the two processes are identical. A solution under pressure is brought into contact with a thin layer of a solid, the membrane. The properties of the membrane are such that the components of the solution pass through the membrane with different velocities, resulting in a difference between the composition of the original solution and the liquid that passed the membrane, the permeate.

If the applied pressure is low (below 1 MPa), the solute to be retained large (MW above 500 Daltons), and the retention by the membrane is thought to be governed mainly by steric factors, not by specific membrane-solvent-solute interactions, the process is usually called ultrafiltration. However, the distinction is quite arbitrary and with many manufacturers, the same equipment is often used for both ultrafiltration and reverse osmosis, the difference being only in the properties of the membrane used. (Gulf, PCI, DDS, UOP-Havens).

1.2. History.

Despite their conceptual likeness the two methods have developed along two very different paths.

According to Ferry's comprehensive review (Ferry, 1936), ultrafiltration of proteins was first reported by Schmidt in 1856.

The name of ultrafiltration, an obvious extension of filtration (from Latin *filtrum*, strainer) had been used for different types of fine filtrations. It was Bechhold, pioneer in the field of preparation and scientific use of collodion membranes, who 1906 coined the term in its presently accepted meaning. Filtrations on macromolecular level have been performed more or less frequently at least since the beginning of the century using a variety of natural and synthetic materials including pig intestine (in the fifties, van Oss found that Western pigs were apparently degenerate and only Chinese pigs would do), collodion and regenerated cellulose. The method was well known to biochemists, but was named most often together with dialysis, and never became very popular.

The phenomenon of osmosis, which is closely connected to the recognition of "semipermeability" of some membranes was studied as early as 1748 by Abbé Nollet. Synthetic membranes were used to study osmotic pressure of sugar solutions 1864 by M. Traube (1867) but if the productivity of ultrafiltration membranes was very low, the transport velocity through the tighter membranes, such as Traube's precipitate of $\text{Cu}_2 \text{Fe}(\text{CN})_6$ in pores of stoneware, was zero to all practical purposes.

In modern times, Reid in 1953 at the University of Florida recognized the potential of the reverse of osmosis for desalination, (Reid, 1972) and experimented with cellulose acetate (Breton 1957, 1958, Reid 1958). However, the fluxes of water through their films were still far too low to be of practical interest. It was Loeb and Sourirajan at the University of California at Los Angeles whose work became a widely quoted landmark in the history of reverse osmosis, when they prepared asymmetric, salt-retentive membranes using Schleicher & Schuell's "UA Ultrafine Superdense Cellulose acetate membranes". They eventually recognized the asymmetry and developed the membrane type that is designated by their names (Sourirajan, 1970). The permeability of the L.-S. membrane was several orders of magnitude higher than that of the previous efforts, and a viable method of separation was thought to be within reach. The Office of Saline Water of the U.S. Department of Interior started supporting a very extensive research program on all aspects

of membrane desalination processes, particularly development of better membranes.

The first attempt to commercialize the new process was by G. Havens, a successful manufacturer of glass-fibre fishing rods, who used his know-how to build modules with membranes cast inside porous glass-fibre tubes. The enterprise failed-whether as a result of inadequacies of the hardware, misplaced emphasis in applications or bad management is hard to judge.

Commercial desalination of sea water, the prime goal of the reverse osmosis research, has not been reached yet. But reverse osmosis is being used in the industry, on full scale, for advanced water treatment. Two large companies, Du Pont and Gulf practically dominate the market. Du Pont gives (Zumbro, 1974) the total capacity sold as 200 000 m³/day.

The interest in reverse osmosis stimulated the interest in the akin process of ultrafiltration. The idea of asymmetric membrane was realized in ultrafiltration membranes by A. Michaels and collaborators and exploited commercially, Maybe because it did not address itself to large scale separations, the Amicon has succeeded better than Havens and became a staple for laboratory ultrafiltration.

1.3. Present situation.

Evidently, membrane separations are not expanding as fast as once expected. Apart from water demineralization, recovery of electrophoretic paints is the only instance where the membrane techniques have gained a sizeable share of the market. There are several technical explanations. For some separations, such as sea water desalination, the membrane that would do the job was not available, or would deteriorate too fast. The engineering of the modules has often not received the same attention as the membranes and equipment failures were frequent. Much of the early research was concentrated on desalination and the equipment was not optimal for concentrating duty, while concentration or fractionation is the goal

of majority of suggested new applications. Finally, the whole problem complex of flux decline on duty has proved to be much more of a difficulty than anticipated.

2. CONCENTRATION POLARIZATION.

2.1. The phenomenon.

In any process for separation of homogenous mixtures, concentration gradients will inevitably arise at phase boundaries. They will be of secondary importance if the phases are fluid and/or the boundary is quickly (at the time scale of the process) renewed. In separations involving a solid phase which stabilizes the gradient, the concentration depletion or enrichment at the boundary often is the cause of serious limitations of the process. The phenomenon was called concentration polarization by analogy to the counterproductive polarization effect of electrochemistry.

Without using the term concentration polarization, Kuhn, 1951, derived the flux decrease caused by concentration polarization at the membrane interface for a pressure driven membrane separation.

During the first modern reverse osmosis experiments, the effects of concentration polarization passed more or less unnoticed. Merten (1963) appears to be the first who took interest in concentration polarization in reverse osmosis and treated it mathematically.

The fact that asymmetric reverse osmosis membranes exhibit rejection only when the less porous, "active" surface of the membranes is facing the feed solution was explained by Banks and Sharples in 1965. It is a consequence of the massive concentration polarization taking place in the porous sublayer of the membrane when this layer is exposed to the feed solution. Gröpl and Pusch (1970) have reached the same conclusion. They succeeded in simulating the behaviour of reversed membrane by applying a nonselective film upon the active surface of an asymmetric membrane.

Three major negative effects of concentration polarization in reverse osmosis are discussed in most general references on the subject - they are effects upon

- osmotic pressure
- rejection
- precipitation

The increased concentration of solute at the feed-membrane interface causes a decrease in the chemical potential of the solvent, as measured in osmotic pressure across the membrane, and a decrease in solvent flux through the membrane at given applied hydrostatic pressure.

At the same time, the higher chemical potential of the rejected solute at the interface gives rise to an increase in its flux through the membrane and thus a decrease in apparent rejection. In ionic membranes, which derive their selectivity from the Donnan effect, the rejection is further reduced by the increased ionic strength of the solution.

Finally, materials of low solubility, such as CaSO_4 and CaCO_3 , may precipitate upon the membrane, causing loss of area available for solvent flux and eventually even damage to the membrane (the experiments reported by Minturn 1973 show however that the connection between flux and rejection decline and sulfate fouling is not as clear as generally assumed).

2.2. Theoretical studies of concentration polarization in reverse osmosis.

Mathematical modelling of concentration polarization has flourished ever since the paper by Merten, going to increasing levels of

refinement. In general, a solution of the coupled nonlinear system of equations of continuity, motion and continuity for a solute i

$$\frac{D\rho}{Dt} = -\rho (\vec{\nabla} \cdot \vec{v}) \quad (1 a)$$

$$\rho \frac{D\vec{v}}{Dt} = -\vec{\nabla} p - [\vec{\nabla} \cdot \tau] + \rho \vec{g} \quad (1 b)$$

$$\frac{D\rho_i}{Dt} = -\rho_i (\vec{\nabla} \cdot \vec{v}) - (\vec{\nabla} \cdot \vec{J}_i) \quad (1 c)$$

(see e.g. Bird, Stewart, Lightfoot (1960))

with the appropriate boundary and initial conditions is sought. Coupling with the properties of the membrane is provided in form of some phenomenological boundary condition relating the trans-membrane flux of solvent to membrane permeability, local hydrostatic pressure, local concentration of solute and solute transport characteristic of the membrane. In overwhelming majority of investigations, the solute transport through the membrane is represented by the solute rejection parameter

$R = 1 - \frac{c'}{c''}$ where c'' solute concentration at the high pressure face of the membrane and c' concentration of the permeate.

A different approach is utilized in the Kimura-Sourirajan analysis (1967) and in subsequent work of Sourirajan and collaborators. The solute transport is described by the solute transport parameter ($D_{AM}/K\delta$), defined as the proportionality constant between solute flux and molar solute concentration difference across the membrane.

In Table 1, modelled after Welinder (1974) the best known treatments of concentration polarization in reverse osmosis are tabulated.

The following simplifications are common to all the references cited, except where indicated otherwise:

- constant properties (viscosity, diffusivity, density)
- binary system
- isothermal system
- no pressure drop in flow direction
- flux proportional to membrane permeability constant and the difference between applied pressure and the osmotic pressure of the solution
- osmotic pressure proportional to solute concentration (van't Hoff's formula)

A most thorough review of the literature up to 1969 is given by Gill et al (1969). Relevant chapters may be found in all monographs on reverse osmosis, eg "Desalination by RO", ed. U. Merten, "Reverse Osmosis Membrane Research", eds H.K. Lonsdale and H.E. Podall, "Industrial Processing with Membranes" eds. S. Loeb and Lacey, "Reverse Osmosis" by S. Sourirajan.

An excellent brief up to date survey is found in the thesis of Welinder (1974).

2.3. Experimental investigations of concentration polarization in RO.

Prior to 1969, the only experimental information on concentration polarization that was available was deducted from the decrease of transmembrane flux and increase of solute concentration in permeate, assumed to be caused by concentration polarization. The techniques are quite coarse, particularly because the characteristics of the membrane may be changing during the experiments. Quite an impressive amount of reverse osmosis test data has been generated, particularly during the latest years. In the following only the studies directed to the assesment of concentration polarization are mentioned.

Turbulent flow in tubular equipment was investigated by Merten et al (1964). Shor et al (1968) used dynamic membranes. Investigations of Kimura and Sourirajan with different solutes are summarized in Sourirajan (1970), Sheppard and Thomas (1970) found concentration polarization in excess of the predicted value and Thomas (1973) had to include an additional eddy diffusivity term to the film model to account for too low concentration polarization at high velocities. Bansal et al 1973 found a modified film model applicable to their data and the data of Richardson et al (1969) and Monge et al (1973). Plain film model is satisfactory to interpret the data of Strathmann, 1972.

In laminar flow, investigations of Strathmann (1968) in slit type channel and their continuation by Bixler and Cross (1969), who even considered the effects of flow maldistribution, confirmed the numerical solution of Brian, 1965 (or more exactly its extension to the channel with one membrane wall, by Strathmann). Laminar flow data were presented even by Bansal et al 1973 - free convection correction could be used to account for the data. Sheppard and Thomas (1970) found good agreement with theory, so did Strathmann (1968 and 1972), Drioli et al, 1973 found varying rejection, so did Welinder 1974. Flux and retention data in unstirred cells were reported by Raridon et al 1966, Williams and Hendrichs 1967, Williams 1969 and Alfani and Drioli 1973. Stirred cell was used for concentration polarization measurements by Strathmann 1968. Data on rotating cylindrical membrane were given by Sherwood, 1967 and rotating disc system was investigated by Kozinski 1971 and Welinder 1974.

Direct observations of the concentration profile were performed for the first time by Liu and Williams (1969). Using electrical conductivity microprobes of 60-75 μm diameter, developed by Hendricks, they were able to follow the concentration build-up in an unstirred cell down to a distance of 0.5 mm from the membrane. The experimental results could be approximated by appropriate theories only in a certain range of experimental parameters. In a study reported by Hendricks and Williams (1971) with improved technique the velocity profile between parallel

plates in laminar flow was measured down to 20 μm from the membrane. They also developed a theory which gave a satisfactory fit to the data. The comprehensive report of Williams et al (1970) gives in addition to microconductometry details of another experimental technique - the shadowgraph, using the changes in refraction index of the solution with concentration, as reflected in the image of a wire in a collimated laser beam. This method however was inferior to the conductivity measurements. An important result of this work is the observation of convectational instability in a membrane channel with membrane on the top.

Goldsmith and Lolachi (1971) used Ag-AgCl electrodes to measure the Nernst potential in NaCl solution. An advantage of the use of Ag-AgCl electrodes compared to the conductivity electrodes of Williams is that these may be in direct contact with the membrane. Reasonable agreement with theory was found for the unstirred cell and laminar flow in an annulus.

Johnson, 1970 used an interferometric technique to follow natural convection in proximity of a vertical membrane.

Recently, Welinder 1974 measured concentration polarization in unstirred cell at steady state with holographic interferometry for a variety of solutes.

Table 1 - Theoretical studies of concentration polarization in RO.

For general assumptions, see text; in addition, letters after references denote:

- a) total rejection of the solute
- b) constant transmembrane flux
- c) buoyancy (free convection) considered
- d) ternary system
- e) variable viscosity
- f) variable diffusivity
- g) multicomponent system
- h) nonideality of osmotic pressure with concentration and solute-solute friction considered

Unstirred batch cell, transient behaviour

Dresner, 1964	a, b
Raridon et al, 1966	b
Nakano et al, 1967	a
Williams, 1967	
Gill et al, 1969	
Goldsmith and Lolachi, 1970	
Johnson, 1971	c
Astarita and Greco, 1970	b
Alfani and Drioli, 1972	

Developed laminar flow between parallel plates

Dresner, 1964	a, b
Johnson et al, 1966	b
Gill et al, 1969	a, b
Sherwood et al, 1963	a, b

Table 1 - continued

Developed laminar flow between parallel plates (continued)	
Ramanadhan and Gill, 1968	b, c
Gill et al, 1965	a
Brian, 1965	
Gill et al, 1966	a
Hendricks and Williams, 1971	
Doshi et al, 1971	a, c, f
Shah, 1969	f
Sherwood et al, 1965	a
Srinivasan and Tien, 1973	
Merson and Ginnette, 1970	a, e
Muhlenkamp and Srinivasan, 1973	a, c
Shaw et al, 1972	
Sourirajan, 1970	
Liu, 1971	
Liu, 1972	
Dresner, 1973	a, b, d, h
Developing laminar flow between parallel plates	
Gill et al, 1966	a
Srinivasan et al, 1967	a
Srinivasan and Tien, 1968	a, d
Srinivasan and Tien, 1970	a, g
Liu, 1971	
Dresner, 1973	d, h

Table 1 - continued

Developed laminar flow inside tubes	
Gill et al, 1969	a, b
Fisher et al, 1969	a, b
Gill et al, 1966	a
Sourirajan, 1970	
Bansal et al, 1973	c
Sherwood et al, 1965	a, b
Developing laminar flow inside tubes	
Srinivasan and Tien, 1967	a
Dresner, 1973	d
Developed laminar flow outside tubes	
Gill et al, 1966	a
Tsao, 1970	c
Developed laminar flow in annuli	
Mastromonico, 1968	b
Gill et al, 1966	a
Winograd et al, 1974	
Tsao, 1971	a, b
Developed laminar flow inside curved tubes	
Srinivasan and Tien, 1971	a
Nunge and Adams, 1973	

Table 1 - continued

Developed laminar flow in shell and tubes
geometry

Winograd et al, 1974

Stagnation flow (axial or planar)

Zeh and Gill, 1967

Chi, 1971

Kozinski and Lightfoot, 1971 a, e, f

Rotating disc

Zeh and Gill, 1968

Kozinski and Lightfoot, 1972 a, e, f

Turbulent flow between parallel plates

Strathmann, 1968 a

Sourirajan, 1970

Doshi, 1967 a

Radial flow cell

Agrawal et al, 1972

Table 1 - continued

Turbulent flow inside tubes	
Sherwood et al, 1961	a, b
Sherwood et al, 1965	a
Brian, 1965	
Winograd and Solan, 1969	
Johnson et al, 1966	b
Sourirajan, 1970	
Bansal et al, 1973	
Thomas, 1973	
Derzansky, 1968	a
Dresner, 1973	d, h
Bansal et al, 1973	c
Turbulent flow inside annuli	
Winograd et al, 1974	
Turbulent flow in shell and tubes geometry	
Winograd et al, 1974	
Stirred cell	
Strathmann, 1968	a
Hollow fibre	
Gill and Bansal, 1973	

3. FLUX DECLINE.

3.1. Causes of flux decline.

Compared to the concentration polarization of simple salts, the other causes of flux decline in reverse osmosis have attracted little theoretical interest. This is easily explained, as the traditional picture of concentration polarization is physically clear-cut and may be a challenging exercise in mathematics, whereas the other causes are poorly understood in physical terms and not as easy to experiment with. Even if the different mechanisms are not readily distinguished, it might be convenient to differentiate conceptually between the effects of

- a) changes in the composition of the membrane material
- b) changes in the transport properties of the membrane by solutes interacting with the membrane material
- c) changes in the physical structure of the membrane backbone
- d) deposition of foreign material on membrane surface

ad a)

All presently commercial membranes, with the exception of Union Carbide's Ucarsep, are manufactured of organic polymers, so is the overwhelming majority of experimental membranes. Of necessity the porous structure of the membranes offers a large surface area and is thus particularly susceptible to chemical attack. The rapid hydrolysis of cellulose acetate below pH 2 and above pH 8 is notorious. However, the deacetylation exerts its deleterious effect on salt rejection, not on flux. After 1 h in nitric acid at pH 0.5 Yi Yan 1973 finds the flux unchanged.

Rosenblatt 1973 warns of effects of chlorine on Du Ponts polyamide membranes.

ad b)

Even if no primary bounds are effected, some solutes interact strongly with the membrane materials. Binding of the solutes may change the hydrophilic character of the membrane matrix or sterically block the passage through the membrane (Lonsdale et al 1967), or alternatively block the surface (Keilin 1964, Kesting and Eberlin 1966).

Phenol is the agent best known to decrease the flux of cellulose acetate membranes and is widely studied because of its negative rejection characteristic (Pusch and Staude 1973, Lonsdale et al 1967, Welinder 1974, Anderson et al 1972, Kesting and Eberlin 1966, Keilin 1964). A large number of compounds, particularly low molecular weight organics, have also been reported to decrease the water flux of RO membranes, clearly beyond any effect attributable to their osmotic pressure. Catastrophic irreversible flux decline may occur with cellulose acetate membranes in solutions of cationic surfactants (Madsen, 1974 a).

Duvel et al 1971 have investigated the effect of 38 organic solutes, mainly alcohols, on cellulose acetate membranes and found large flux declines (20-30 %) for 1-hexanol, benzylalcohol, 1-heptanol, 2,4 dimethyl - 3-pentanol, 2-phenyl-ethanol, 1-octanol and 3-phenyl-1-propanol. They conclude that significant flux declines are caused by organics with more than 5 carbon atoms. However, for higher solute concentration (1 % w/w) Kesting and Eberline found large flux losses with smaller organics-linear 3 and 4 carbon acids, alcohols, aldehyds etc. Palmer et al 1973, compared anionic, cationic and nonionic surfactants on polysalt and cellulose acetate membranes. They found specific flux decreasing interactions between Triton X-100 (octylphenolpolyethyleneoxide) and cellulose acetate. These were reversible. The polysalt membrane interacted irreversibly with Hyamine 3500 (N-alkyldimethylbenzylammonium chloride - 50 % C₁₄, 40 % C₁₂, 10 % C₁₆) According to Michaels 1973, microcations of the membrane are exchanged for the surfactant, with resulting dehydration and densification of the membrane.

Chian and Fang 1973 investigated the rejection of organics, by

some newly developed RO membranes, concentrating on organics which are poorly rejected by cellulose acetate membranes. Definite flux loss was found with North Star's NS-1 noncellulosic polymer in solutions of urea. There might be some flux loss for ethyl ether solution for both NS-1 and Chemstrands polyamide.

ad c)

The structure of the membrane is known to change under pressure. Creep, the plastic deformation under long-term stress, a common phenomenon, very pronounced in polymer materials, is continually densifying the membrane. There is some disagreement as to what part of the structure is responsible for the observed flux decline. Baayens and Rosen, 1972 implicate the active layer.

King et al 1972, list the densification of the porous structure, increase of thickness of the dense layer and densification of the dense layer as probable possibilities.

Various strategies for diminishing the compaction have been used. The composite membrane concept, initiated at Gulf General Atomic (Riley et al, 1967) and North Star (Francis, 1966) is the most prominent approach, but other methods, such as inorganic fillers (Deanin et al, 1970, Baum et al, 1972) grafting of creep resistant polymers (e.g. Kimura-Yeh et al, 1972) or cross-linking (Hoernschmeyer et al, 1972) are being investigated.

Embossing of the support material structure into the membrane, amply shown in literature (Rosenblatt, 1973, Sheppard and Thomas 1970) affect the flux via the secondary effect of concentration polarization in the stagnant depressions of the membrane (Carter et al, 1974).

Solutes interacting in a high degree with the membrane material may alter the structure of the membrane (Peri et al, 1973) up to the point of dissolving the polymer (Sourirajan 1970. p. 409-428).

3.2. Membrane fouling

Membrane fouling, the deposition of solutes on the surface of the membrane, exerts its effect on membrane flux in two ways - directly as a hydraulic resistance, and indirectly via the increased concentration polarization in the stagnant boundary layer caused by the deposits.

Some evidence of fouling may be found in all reports on long-term use of reverse osmosis equipment, but it is most spectacular in systems such as milk and whey or paper and pulp wastes, where flux may decline to half its original value during a few hours.

Extensive data on fouling may be found in any of the larger studies designed to investigate optimal process management for a specific separation problem e.g. Wiley et al, 1972, for paper and pulp effluents, Fenton-May 1971, Peri and Dunkley 1971 for whey, Peri and Pompei 1972 for milk.

Work done to study specifically the fouling phenomenon is less common.

Fouling may be caused by a variety of compounds. Leiserson (1973) lists

- heavy metal oxides
- bacterial slimes
- CaSO_4 and CaCO_3
- organic colloids
- inorganic colloids

Very often, several types of compounds are encountered together. This is not always clear from the reports, as it is seldom possible to identify all of the deposits.

Iron is regularly found in the deposits from water and sewage treatment if an iron coagulation step is a part of the pretreatment (Kuiper et al 1973, Cruver and Nusbaum 1974) or iron is pre-

sent in the feed originally (McCutchan and Johnson 1970, Grover and Delve, 1972). Corrosion products were found even in a stainless steel test loop, Carter et al, 1974, and in Monel 400 equipment, Agrawal et al 1972. Bishop, 1970 reports besides iron even 3,8 % lead in deposit from concentrated primary effluent at Pomona.

Microbial slimes were found, together with pitch, by Wiley et al, 1972 in deposits from wash water from calcium acid sulfite pulping of sprucewood. Feuerstein and Bursztynski 1971 observed "thick fluffy green organic growth" from alum treated sand filtered primary effluents. The green colour is surprising in case the deposit was resident.

Feuerstein reports also that massive CaSO_4 fouling occurred when pH of primary sewage was adjusted by sulfuric acid and the unit run at high recovery. A deposit consisting almost entirely of CaSO_4 was found by Beckman et al 1973 in a spiral module working on polluted surface water. The precipitation was apparently caused by a failure of the brine side seal which gave maldistributed flow.

"Organic material" is the category that appears most frequently in reported deposit contents. It is seldom identified. Lim et al, 1971 were able to determine high content of a casein in deposits from processing of whey. Cruver and Nusbaum 1974 found mainly polyhydroxy aromatics in deposits from waste water treatment and Beckman et al 1973 reported 26 % organic acids and 44 % polysaccharides from polluted surface water.

The proportions of organic material in deposits are often surprising. Grover and Brooker 1974, studying in electron microscope the deposits from milk concentration found most of the deposit inorganic, with protein accounting for 30 % only. On the other hand, Minturn, running with simulated brackish water, found a B9 permeator deposit to contain 67 % of organics, in spite of the fact that nominally the only organic material entering the unit

were the citric acid and EDTA solutions used for cleaning. Bevege et al (1973) mention that deposit from a module treating plating wastes consisted of 45 % organics.

Hayes et al 1974 found that calcium phosphate is involved in fouling when processing whey. Si, Ca and P are often found in waste water deposits, but the nature of compounds involved beyond SiO_2 is hard to reveal. A typical observation might be the one of Bashow et al 1972. Their hollow fibre modules became excessively fouled by trickling filter effluent, despite thorough pretreatment- sandfilter, 50 μm filter in series. The deposit is described as partly greasy, partly amorphous organic and partly crystalline. The crystalline material consisted mainly of Ca and P but did not fit any conceivable formula.

3.3. Experimental investigations of membrane fouling.

In a series of papers from the Oak Ridge National Laboratory (Sheppard and Thomas 1970, 1970 a), 1971, Sheppard et al 1972, Thomas and Mixon 1972) the phenomenological aspects of fouling with river water and primary sewage were investigated extensively. They found that fouling may be associated with flux loss, rejection loss or both. For a given feed, flux decline with time is increased for membranes of higher initial flux. Pretreatment, such as filtration and acidification, has a large beneficial effect on flux decline rate. Tangential flow decreases fouling substantially. The major finding of this series of investigations is that for every feed there is a threshold velocity which gives a sharp decrease in fouling.

Kuiper et al, 1973 reported a long-time test series on Rhine River water. Their results parallel those of the Oak Ridge group. Fouling is decidedly diminished at higher tangential velocities (2 m/s) and high-flux membranes are fouled more extensively. In course of the investigation it was found that iron in the membrane

deposit makes subsequent foam ball cleaning easier.

Another large fouling study was performed by the Gulf group (Beckman et al, 1973). Different modifications of spiral wound modules were tested on highly polluted surface water with varying pretreatment and hydraulic regimes. Severe flux decline was observed for high flux membranes. The effect of increased tangential flow, while clearly beneficial, was not as pronounced as the effect of transmembrane flux in the rather low velocity range investigated. An attempt was made to correlate fouling with the characteristics of feed, but no definite answers were found. High turbidity is always associated with high fouling rate, but not vice versa. The silting index, an empirical filtration procedure defined by SAE ARP 788 had some predictive value, so had ultraviolet absorbance at 275 nm, total organic carbon and chemical oxygen demand. (- Interestingly, not the biological oxygen demand which was interpreted as predominant presence of refractory organics in the feed water)

Three studies specifically designed to study membrane fouling in reverse osmosis under controlled conditions were located in literature.

Jackson and Landoldt, 1973, used small amounts (40 ppm Fe) of iron hydroxide with 5000 ppm NaCl in titanium equipment for tests of short duration. The amount of deposits was inferred from the concentration of Fe in the circulating solution. As expected, fouling (the amount of Fe deposited on the membrane) is sensitive to flow velocity, with large decrease in fouling rate at Re 20 000 corresponding to linear velocity of 0.8 m/s. Traces of oil aggravated the fouling considerably. In every experiment, fouling is a smooth function of tangential flow, but the absolute amount of deposit varies considerably between nominally identical experiments. Experiments at different pH showed more fouling at high pH (11-11,5) than at low pH (3-3,4) and the least fouling close to neutral. This is explained as an effect of formation of large coagulated particles at isoelectric pH, which are easily swept away from the

membrane. There is no direct proportionality between the amount of deposit and flux decrement.

Minturn 1973 followed visually the build up of calcium sulfate crystals in a transparent annular test apparatus equipped with cellulose acetate membranes. Flux decreases coincide with the appearance of crystals and flux improvement with crystal dissolution. There were some indications that at high velocities (10 m/s), no crystals were deposited even from saturated solution. Conversely, high velocity by itself did not suffice to bring crystals already formed into a solution that was relatively close to saturation. The reported data do not allow any quantitative conclusion on the relationship between the amount of deposit and flux.

Minturn has also performed tests with commercial modules and simulated brackish waters. Even in this part of the study, supersaturated solutions exiting from the modules were encountered.

Researchers from Gulf (Bevege et al, 1973) reported a study devised to simulate the fouling behaviour of surface waters. They used various combinations of humic acids, bentonite clay, NaCl plus divalent and trivalent cations in trace amounts to evaluate the effect of component interactions, membrane characteristic, pressure and flow rate on fouling of spiralwound modules. They showed that the applied pressure and the membrane permeability per se did not influence the fouling significantly. The often observed rapid fouling of high flux membranes may be attributed to higher permeate fluxes. The fouling rate differed for different tangential velocities (recovery ratios) only for feeds of low fouling capacity. The effect of filtering was confirmed (3 times less flux decline). The effect of interactions between humic acid and clay was striking, and even more the interaction between humic acid and multivalent cations. Fouling (flux loss) rates 10 times faster than with only humic acids occurred on additions of ppm amounts of Al. Ca and bentonite had somewhat less disastrous effect.

The behaviour of humic acids + multivalent ions is interpreted as destabilization of the polyelectrolyte on neutralization with

the polyvalent cations - the neutralization is confirmed by measurements of streaming potential. However, no neutralization was found in measurements on bentonite - humic acid interaction (both negatively charged). An alternative mechanism, adsorption of humic acids on bentonite, leading to fouling by the large particles formed was proposed.

3.4. Measures to prevent fouling.

In general, three approaches to the fouling prevention may be discerned. These are concerned with:

- a) the properties of the feed
- b) the hydrodynamics of the module
- c) the properties of the membrane

ad a)

It has been amply demonstrated that removal of all particulates from the feed is advantageous. With few exceptions (Conn, 1971), reverse osmosis equipment is being protected by fine filters down to 5 μm . Potentially troublesome compounds are if possible eliminated in advance by treatments such as chemical coagulation, adsorption on active carbon, chlorination and pH adjustment. Even complexation of scale - building salts and the use of organics scavenging macroporous ion exchange resins has been contemplated. When working with process streams, the elimination of aging of the feed may be of paramount importance (see e.g. Wiley 1972). Work on potato starch effluent in this department has shown doubling of flux when fresh effluent is used (Sivik 1974, Eriksson 1975).

ad b)

All the measures that decrease concentration polarization are expected to decrease fouling. The advantages of working with high tangential velocities are obvious from the published data. However, there is a number of distinct disadvantages in this concept. The major ones are high energy losses and the need for high

recirculation ratios.

No satisfactory comparison of fouling proneness of turbulent, high velocity and laminar, thin channel systems is known to this author, but Madsen (1974 b) estimates that the fouling is equal at equal wall shear rate. If the reasoning on energy costs of concentration polarization management put forward by Blatt et al 1970 is found applicable to fouling, laminar system should be energetically advantageous.

In addition to the different channel forms a number of inserts into the flow channels of modules have been proposed. A general objection to all of these is that energy might be more usefully dissipated at the membrane surface than at the inert surface of the inserts but again, no experimental proof exists.

American Standard had used slightly undersize balls in their commercial modules, and Havens (now Fluid Dynamics Division, Universal Oil Products) has been using spirally twisted volume displacement rods to increase turbulence.

Delached wires as turbulence promoters were extensively investigated at Oak Ridge (Thomas and Watson, 1968, Thomas et al 1970).

An optimization study of Thomas et al 1971 concludes that the major positive effect of turbulence promoters in desalination would be in reducing fouling.

Lowe and Durkee, 1971, proposed for food applications undersize balls aided by alternating flow. The use of Kenics Static Mixer, a proprietary turbulence promoting insert was investigated by Pitera and Middleman 1973 and Copas and Middleman, 1974. The effectiveness of similar inserts and Havens volume displacement rods was compared by Dejmek et al 1974.

Hollow fibre modules with membranes at the outer surface of the fibre are notorious for poor fouling properties. A major improvement might be the design tested on filtered effluent by Bashaw et al, 1972. In this module, a fabric, woven of hollow fibre yarn with cotton warp, is rolled on to a central mandrel and used instead of the customary fibre bundle.

Lai and Nickelson, 1971, proposed the use of fluidized bed inside RO modules. Lolachi 1973 reported some very impressive results with this technique. The long term effects of the fluidized particles on the membrane are not known.

The researchers of Westinghouse (Gross et al, 1972) and Dejmek and Hallström 1974 proposed frequent (up to 10 times per minute) backpressure wash of the membrane with promising results. Even these methods might however induce intolerable strain on the membrane.

ad c)

The membrane modifications proposed might be designated "non-fouling" and "self-cleaning". Non-fouling membranes are based upon the assumption that negatively charged colloids of the feed are a major fouling factor. A negatively charged membrane should repel the colloids and ensure fouling-free service. So a cellulose acetate-hydrogen succinate membrane was tested on Pomona secondary effluent, giving 15.5 gfd with no flux decline under the first 6 days. (Fisher and Lowell, 1970) and antifouling properties are ascribed to highly sulfonated membranes prepared by "a witch brew, usually of a sulfonic acid polymer, matrix polymer and cross linking reactions" (Gregor, 1973).

The preparation of self-cleaning membranes was investigated by Fisher and Lowell, 1970 and Dejmek, 1972. Fisher and Lowell attached trypsin to a membrane cast from cellulose acetate-N-hydroxy-succinimide. The membrane showed activity towards BAEE, but no actual tests with the membrane were reported. In our independently initiated study, trypsin was bound to a cellulose acetate membrane by the cyanogen bromide method. In spite of proved proteolytic activity, the membranes did not behave differently from controls in runs with proteinaceous solutions and did not even recover faster after fouling.

4. CONCENTRATION POLARIZATION IN ULTRAFILTRATION.

4.1. Introduction.

In the formal definition of the problem, concentration polarization in ultrafiltration does not differ from concentration polarization in reverse osmosis, see above. However, in ultrafiltration, the rejection of low molecular weight compounds is generally low and concentration polarization behaviour is likely to be determined by the properties of macromolecules in solution. In comparison to solutions of simple salts, solutions of macromolecules present low osmotic pressure, and high, concentration dependent viscosity or even more complex rheological behaviour.

The self-diffusion coefficients of macromolecules are low and concentration dependent. Thus, it would be surprising if the "constant property" simplifications of the fundamental theory of concentration polarization in reverse osmosis were acceptable in treatment of ultrafiltration. Any theory of concentration polarization in ultrafiltration must be able to explain the observed behaviour. A major practical difference between reverse osmosis and ultrafiltration is the dependence of flux on pressure. In reverse osmosis, flux increases with pressure more or less linearly. In ultrafiltration after an initial increase, flux becomes roughly independent of pressure.

In the following, the significant contributions to the theory of concentration polarization in ultrafiltration will be summarized.

4.2. The Amicon group treatment.

This approach is based upon the work of Bixler et al 1968 and was comprehensively presented in Flinn's book (Blatt et al. 1970). The key concept of the theory is the gel concentration. If the total convective flux of solute towards an element of a solute rejecting membrane exceeds the diffusional and convective flux away from the membrane, the solute concentration at the surface

will rise. Eventually, the highest possible concentration, the "gel concentration" might be reached and instead of increasing concentration, the thickness of the concentrated layer will increase. This layer offers large hydraulic resistance to the transmembrane solvent flux and makes it selflimiting.

No amount of pressure will increase the steady state flux, because increased pressure will only lead to increased accumulation of the concentrated layer.

Thus when "gel concentration" is reached, the diffusive back-transport cannot be further increased.

Formally, these workers make use of the boundary layer theory to integrate the one-dimensional steady state equation of mass transport of the totally rejected solute,

$$v c - D \frac{dc}{dx} = 0 \quad (2)$$

across concentration boundary layer of thickness δ , assuming constant properties of the solution to get

$$\ln \frac{c_w}{c_b} = v \frac{\delta}{D} \quad (3)$$

The equation may be interpreted as a definition of the mass transport coefficient k

$$\ln \frac{c_w}{c_b} = \frac{v}{k} \quad (3 a)$$

The values of the mass transport coefficient k are to be ascertained for different flow regimes.

In fully developed laminar flow with developing concentration boundary layer, the Leveque solution, assuming constant shear stress in the thin layer, constant properties, and neglecting mass transfer, originally developed for heat transfer, is applied

$$k = B' \left(\dot{\gamma}_w \frac{D^2}{L} \right)^{1/3} \quad (4)$$

where B constant depends on geometry and wall boundary condition.

In turbulent flow, the familiar power relationship

$$Sh = \frac{k d_h}{D} = A Re^a Sc^b \quad (5)$$

is used.

In stirred cell, the preferred mass transfer coefficients are given by

$$\frac{kr}{D} = 0.285 \cdot Re^{0.55} \cdot Sc^{0.33} \quad (6)$$

for laminar flow, with the Reynolds number based on stirrer angular velocity and cell radius ($Re = \frac{\omega r_D^2}{\eta}$) between 8000 and 32 000

In turbulent regime, $32\,000 < Re < 82\,000$

$$\frac{kr}{D} = 0.0443 Re^{0.75} Sc^{0.33} \quad (7)$$

is suggested.

If the "gel concentration" is reached, eq. 3 a plus the appropriate mass transfer coefficient should determine the flux, irrespective of the applied pressure difference across the membrane. As long as the wall concentration is below the "gel concentration", the flux is determined by the applied pressure, the permeability of the membrane and the permeability of the polarized layer close to the membrane. The last two may be interpreted as two hydraulic resistances in series,

$$v = \frac{p}{m_m + m} \quad (8)$$

where m_m hydraulic flow resistance in the membrane and m flow resistance in the polarized layer.

The m is a function of the concentration profile and increases with increasing applied pressure. In a typical plot of flux versus pressure, Fig. 1, m_m and m are identified graphically for a given permeate flux

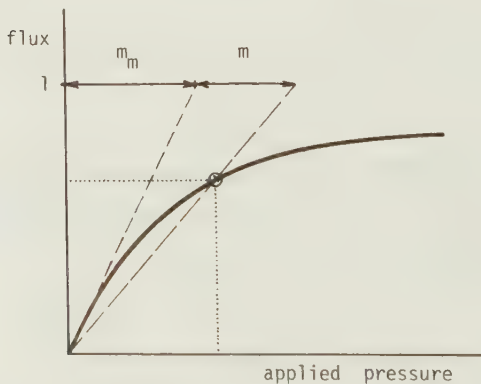


Fig. 1. Flow resistance of membrane and boundary layer.

4.3. Work at Albany.

Ginnette and Merson at Western Regional Research laboratory of USDA presented a model for calculations of the limiting flux obtainable in processing of viscous liquids in a channel between two parallel membranes. Originally, they assumed a membrane of infinite water permeability, but the model was later extended (Merson et al, 1968) to include the effect of flux resistance across the membrane. Eq. 1c is simplified to

$$u \frac{dc}{dx} + v \frac{dc}{dy} = D \frac{d^2c}{dy^2} \quad (9)$$

that is, stationary two dimensional mass balance of a solute, neglecting axial diffusion and the concentration dependence of diffusion coefficient.

Linear distribution of shear stress in the channel is specified and a power law representation of fluid viscosity, taking account of solute concentration, is used. The assumption of no flux resistance in the membrane ($m_m = 0$), together with the usual transmembrane flux formula

$$v_w = \frac{1}{m_m} (p - \pi_w) \quad (10)$$

gives rise to the boundary condition that solute concentration at the membranes be such that $p = \pi_w$.

Fully developed laminar flow is assumed in channel entrance.

4.4 Work of the Hydronautics group.

The paper of Brown et al, 1971 is in spirit somewhat akin to the Amicon work. Here again the osmotic pressure of the solution is disregarded. Gelling of the concentrated layer is recognized as physical limitation of the transmembrane flux. The solution is numerical, based upon the work of Sherwood, Brian and Fisher (1963) and in the same geometry, thin channel with membrane on both walls. The flow is laminar. Concentration dependence of viscosity and diffusivity is taken into account as

$$\eta = \eta_0 e^{Kc_0 \left(\frac{c}{c_0} - 1 \right)} \quad (11)$$

and

$$\frac{D}{D_0} = \frac{\eta_0}{\eta} \quad (12)$$

the Leveque simplification of constant shear stress in the boundary layer is made, together with the usual assumptions of stationary state, no axial diffusion and constant pressure at every cross section of the channel. The equations (1) simplify to

$$\frac{du}{dx} + \frac{dv}{dy} = 0 \quad (13 a)$$

$$\eta \frac{du}{dy} = \eta_0 \left(\frac{du}{dy} \right)_0 \quad (13 b)$$

$$u \frac{dc}{dx} + v \frac{dc}{dy} = \frac{d}{dy} \left(D \frac{dc}{dy} \right) \quad (13 c)$$

For boundary conditions, zero slip and balance between convective and diffusive flux at the wall are specified.

Two cases are considered:

A given flux, constant along the channel. The solution is given in form of a diagram of wall concentration vs the dimensionless channel length ζ introduced by Dresner, here defined as

$$\zeta = \frac{x v_w^3 \eta_0}{D_0^2 \tau_0} \quad (14)$$

with the viscosity exponent Kc_0 of eq. 11 as a parameter. A notable point of the relationship is that for every non zero Kc_0 there is a value of ζ where the wall concentration steeply rises to infinity, the incipient gelling point.

"Gel concentration" reached along the channel. The constant flux boundary condition was here replaced by a constant wall concentration, and the flux allowed to vary along the channel. The equation system could be reduced to an ordinary differential equation by a transformation of variables and solved by a finite difference method. In limit, when the wall concentration approaches infinity, the local flux is given by

$$v_w = \left(\frac{D_0^2}{3x} \frac{du}{dy} \right)^{1/3} V \quad (15)$$

and V is function of the viscosity exponent Kc_0 only.

Thus both solutions predict a maximum value of the ζ parameter, which might be interpreted as a maximum of the average flux for a given channel, flow conditions and solution. For a 100 fold variation of the viscosity exponent Kc_0 , corresponding to a 10^4 variation

of the maximum, the difference between the incipient gelling and the total gelling is quite small, mere 15 % increase in average flux.

4.4. The work of Gill and associates.

As seen in chapter 2.2, this group has done a great deal of the mathematical development of the theory of concentration polarization in reverse osmosis. An approach to the problem of processing a two component system with variable properties was summarized in the paper by Doshi, Dewan and Gill, 1971.

The problem is formulated between parallel plates in fully developed, laminar flow of constant density fluid at steady state, neglecting axial diffusion. In addition to Eq 13 a and 13 c, it is assumed that

$$v = v_w(x) \cdot f(y) \quad (16)$$

that pressure drop across channel is negligible and that the permeation flux affects the pressure drop along channel only via the decrease of axial velocity, so that Eq 1 b reduces to

$$\frac{\delta p}{\delta x} = \rho \frac{\delta}{\delta y} \left(\eta \left(1 - \int_0^x v_w dx \right) \frac{d^2 f}{dy^2} \right) \quad (17)$$

From this equation and the appropriate boundary conditions (no slip at wall and symmetry) the velocity field as a function of v_w is found and from the velocity, via viscosity, the concentration field.

The concentration dependence of viscosity and diffusivity is represented as

$$\frac{D}{D_0} = \frac{\eta_0}{\eta} = \left(\frac{1 - B_0 \frac{c}{c_0}}{1 - B_0} \right)^{2.5} \quad (18)$$

The assumption of Eq 16, however, limits the utility of the solutions derived. 3 ways of solution are attempted: an integral method, assuming a second order polynomial for the concentration, a Leveque - type solution, neglecting transverse convection and linearizing the velocity profile at wall and the method of rapidly varying boundary condition, assuming constant shear stress in the part of the boundary layer close to the wall and constant viscosity and diffusivity in every cross section of the channel.

The Leveque solution does not converge for other conditions than the immediate vicinity of channel entrance. The last assumption of the method of rapidly varying boundary condition seems to be very unrealistic for macromolecular solutions. Finally, the integral method is apparently satisfactory when the effect of osmotic pressure of the solution prevails over the effect of varying physical properties of the solution.

4.5. The work of Kozinski and Lightfoot.

In a series of papers, Lightfoot and associates considered the problems of ultrafiltration with particular respect to the complex properties of macromolecular solutions. The geometries studied were two dimensional stagnation flow and flow about rotating disc, but an extension to arbitrary geometry was discussed.

In the paper of Kozinski and Lightfoot, 1971, stagnation flow is considered. The variations of diffusivity and viscosity are correlated as

$$\frac{D}{D_0} = \frac{\eta_0}{\eta} = 1 - Kc \quad (19)$$

The differential equations 1a and 1c are reduced to Eq. 13a and 13c with the same assumptions, but 1b is simplified to

$$\frac{\eta}{x} \frac{du}{dy} = \tau_{\infty} \quad (20)$$

i.e. shear stress independent of y inside the thin concentration boundary layer. The value τ_{∞} is found by matching with the known exact solution of the problem for constant properties. The problem is similarity transformed to one-dimensional and solved numerically. The somewhat surprising conclusion is not only that the form of concentration dependence of viscosity and diffusivity is of little importance in predicting the sludging behavior, but even that the variation itself has very small effect.

For "gelling" the mass transfer is given as

$$Sh \triangleq 0.5 \left(\frac{c_w}{c_o} \right)^{0.4} Re^{1/2} Sc^{1/3} \quad (21)$$

and the groups are evaluated at bulk conditions, $Re = \frac{uX}{\nu}$

In the thesis of Kozinski (1971) and the corresponding paper (Kozinski and Lightfoot, 1972) the transport of solvent through the polarized layer is treated at first generally. A formula for the diffusion of solvent through the boundary layer, taking account of actual body forces and chemical potential, derived from Scattergood and Lightfoot 1968, is given as

$$N_s - X_s (N_p + N_s) = C_m D_{ps} \left(\left(1 + \frac{\delta \ln \gamma_s}{\delta \ln X_s} \right) \frac{\delta X_s}{\delta y} + \right. \\ \left. + X_s \frac{\bar{V}_s}{RT} \frac{\delta p}{\delta y} \right) \quad (22)$$

where Θ_{ps} is the pseudobinary isobaric protein-solvent diffusion coefficient, D_{ps} , corrected for variations of water activity

$$D_{ps} = \left(1 + \frac{\delta \ln \gamma_s}{\delta \ln X_s}\right) \Theta_{ps} \quad (23)$$

The transport coefficient of pressure diffusion $C_m \Theta_{ps} X_s \frac{\bar{V}_s}{RT}$ seems however to be identified with the hydrodynamic resistance of an eventual gel layer. Such a procedure appears not to find support in e.g. the treatment of membrane transport in the monograph of Schlögl (1964) or other work (Merten, 1966). It was shown by Kuhn (1951) that the two coefficients, may be identified only in case of dense membrane, with pore size of the order of size of permeant molecules, such as the membrane of the article of Scattergood and Lightfoot.

To account for the flattening of the flux vs pressure curve in ultrafiltration, three possibilities are listed:

- 1) the osmotic pressure rising to infinity at finite concentration
- 2) increasing thickness of deposit
- 3) compaction of deposit

In analysis of the rotating disc system (Kozinski 1971, Kozinski and Lightfoot 1972) the mass balance of solute takes form

$$v \frac{dc}{dy} = \frac{d}{dy} D \frac{dc}{dy} \quad (24)$$

with the same assumptions as before. Constant shear stress throughout the boundary layer is assumed, matching the shear stress outside the boundary layer. In addition to a solution fully parallel to the previous paper and giving comparable results, the problem is solved even for an asymptotic expansion and numerically,

taking into account the actual properties of a protein, bovine serum albumin. The asymptotic solution assumed a linear concentration profile at the membrane and a linear approximation of solution properties at the membrane. The solution may be converted to a form similar to Eq 21

$$Sh = \left(\tau_0 \frac{c_w}{c_0}\right)^{1/3} \left(\frac{x_{D_w}}{x_{\eta_w}}\right)^{1/3} Re^{1/2} Sc^{1/3} (\text{correction terms})^{1/3} \quad (25)$$

where x_{D_w} and x_{η_w} are dimensionless properties and the correction terms describe the variation of the properties with distance from the membrane. In comparison with experimental data however, instead of

$$\left(\frac{x_{D_w}}{x_{\eta_w}}\right)^{2/3} \cdot (\text{correction terms})^{1/3}$$

$$\left(\frac{x_{D_{ave}}}{x_{\eta_{ave}}}\right)^{1/3}$$

with average dimensionless values between bulk and wall were used.

The numerical solution was found to be extremely sensitive to the actual physical property behaviour at high protein concentration. However, it showed excellent agreement with experimental data for a set of experimental conditions.

Based upon their work on rotating disc flow, Kozinski and Lightfoot analyzed the thin channel flow. The result arrived at by a similarity transformation is applicable to the fully "gelled" region, that

is the limiting flux, assuming the shear stress to be equal to the shear stress without mass transfer. Their final formula for the mass transfer is

$$Sh = \frac{v_w \cdot L}{D} = Sc^{1/3} Re^{1/3} \left(\frac{3L^2}{2hx} \right)^{1/3} \left(\frac{c_w}{c_o} \frac{x_{Dw}^2}{x_{nw}} \right)^{1/3} \cdot (\text{corr.terms})^{1/3} \quad (26)$$

4.6. The work of Porter.

Porter (1972) has reviewed the "Amicon approach". In addition he put forward an explanation to the enormous discrepancy found e.g. by Blatt et. al in comparing the fluxes of colloidal size suspensions to the predictions based on the diffusional back transport theory. Porter shows that the augmentation of the apparent diffusion coefficient is caused by what he terms "tubular pinch effect" - the radial migration observed in suspensions, which leads to a particle - depleted zone near the wall in laminar flow in tubes. Examining the various formulas given by hydrodynamicians he finds that the migration velocity v^* is given by

$$v^* = \text{constant} \cdot u \cdot Re \cdot \left(\frac{r_{\text{particle}}}{r_{\text{channel}}} \right)^{k_1} \cdot f(\text{radial position}) \quad (27)$$

with the exponent k_1 assuming values between 2.84 and 4 and the function f has maximum at the channel wall.

4.7. Some comparisons between theory and data.

Goldsmith (1971) published data on ultrafiltration of several dextran fractions and a polyethylene glycol in tubular turbulent flow, thin channel and stirred cell. The data is analyzed on basis of the assumption that osmotic pressure is limiting the flux. Thus out of flux impairment the osmotic pressure and the corresponding wall concentration is calculated. (eq. 10). The definition of mass transfer coefficient, Eq. 3a is expanded to take into account incomplete rejection

$$v = k \frac{c_w - c_{perm}}{c_b - c_{perm}} \quad (28)$$

and the mass transfer coefficient is calculated. For both laminar and turbulent flow, at a given velocity and varying concentrations, k values are more or less constant. Reanalyzing the data, it might be shown that if the alternative explanation of hydrodynamically limited flux is used, the k values are approximately the same but show less scatter. The constancy of k suggests that the usual type of correlation of the type of Eqs 5, 29 and 30 with the dimensionless groups evaluated at bulk concentration is invalid.

The correlation

$$Sh = 0.0096 \, Re^{0.913} \, Sc^{0.346} \quad (29)$$

when evaluated at bulk properties predicts much higher k than the flux data allow and underestimates k when the estimated wall properties are inserted.

On the other hand, an analogy to Grober's expression for heat transfer in developing laminar flow

$$Sh = 0.664 \left(Re \frac{d}{L} \right)^{1/3} Sc^{1/3} \quad (30)$$

agrees quite well with the data when bulk properties are considered at the lowest concentration measured, but again the expected decrease of mass transfer with increasing concentration is not observed. The 0.5 power of velocity, appropriate to this short channel, is confirmed.

In the stirred cell, the plot of flux vs log of concentration is linear, implying mass transfer coefficient independent of bulk concentration despite a 7 fold increase in bulk viscosity. The linear extrapolations to zero flux correspond however to osmotic pressures which are multiples of the applied pressure.

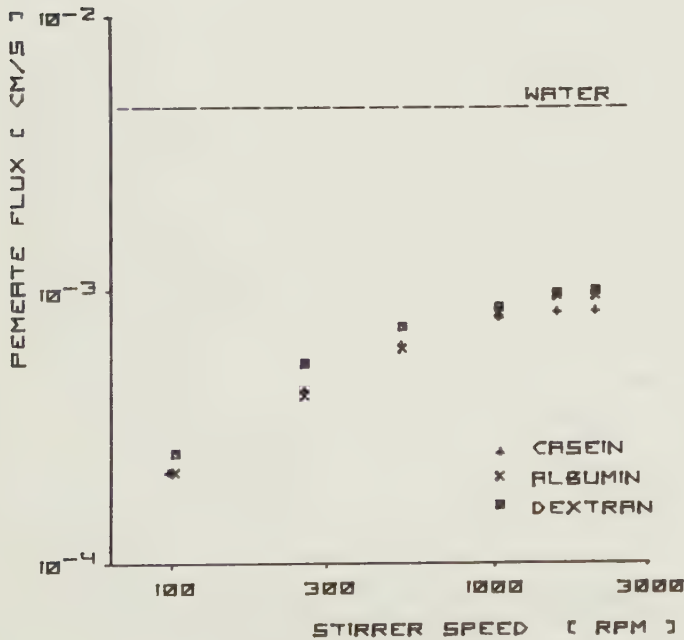


Fig. 2: Permeate flux of macromolecular solutions and of pure water. Data of Strathmann 1973.

Strathmann (1973) analyzes his data according to the Amicon work. Quantitatively, some surprising results are reported in a stirred cell, Fig. 2. An increase of stirrer speed above 1000-1500 rpm brings about no improvement of permeate flux for 1 % solutions of casein, albumin or MW 110 000 dextran, but the flux is still at only 15 % of pure water flux. The extrapolated "gel concentration" of hemoglobin is 3.4 %, according to Strathmann's fig. 11.

The results with 1 % hemoglobin solution in thin channel with turbulent flow, at different pressures, velocities and channel heights are replotted here in Fig. 3. The mass transfer coefficient is calculated, as proposed by Strathmann, from the formula

$$Sh = 0.023 Re^{0.8} Sc^{0.33} \quad (31)$$

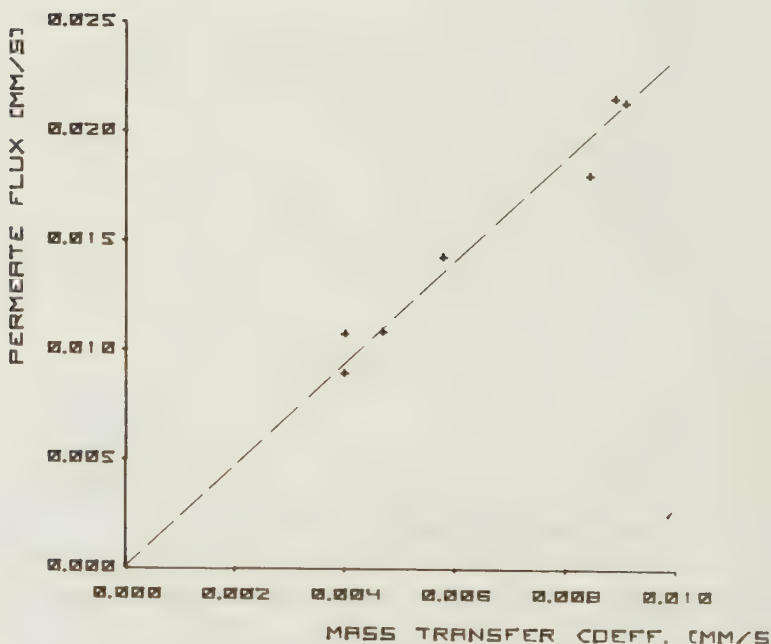


Fig. 3: Permeate flux of 1% hemoglobin in turbulent flow cell, data of Strathmann 1973.

As predicted by Eq. 3a,

$$v = k \ln \frac{c_w}{c_b}$$

flux is proportional to the calculated mass transfer coefficient, and independent of pressure, which of course means that the gel concentration at wall was reached. However, the numerical value of the gel concentration, 10 %, is definitely too low.

In laminar flow

$$Sh = 1.86 (Re \ Sc \frac{h}{L})^{1/3} \quad (32)$$

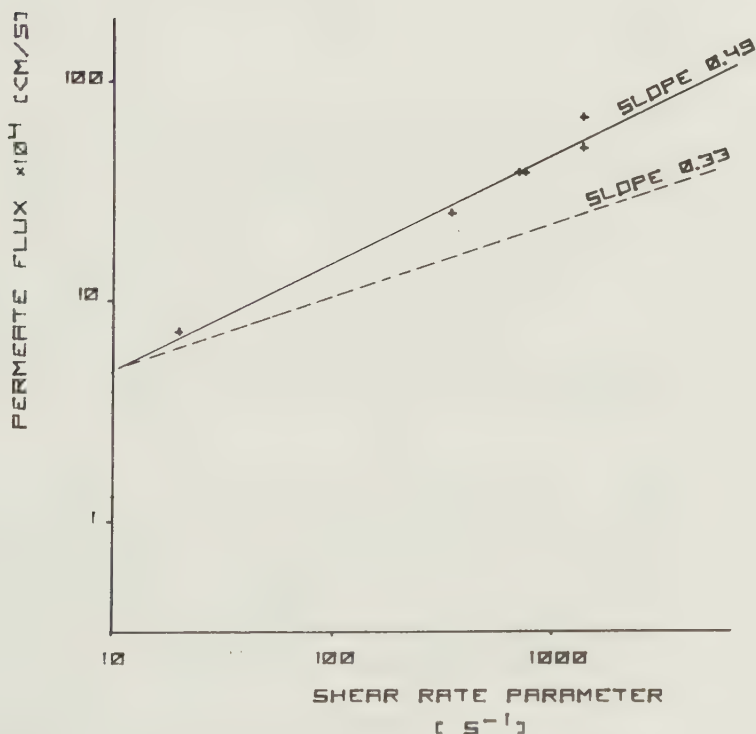


Fig. 4: Permeate flux of 1% hemoglobin, laminar flow cell, data of Strathmann, 1973

or in form Eq 4

$$k = 1.86 \left(\frac{u}{h} \frac{D^2}{L} \right)^{2/3} \quad (32a)$$

Replotting the data as in Fig. 4, it is seen that the dependence of flux on the shear rate parameter $\frac{u}{h}$ is closer to 0.50 than the predicted 0.33. (Incidentally, Fig. 10 of Blatt et al, 1970, gives the slope 0.42 in case of laminar flow in a stirred cell). When the mass transfer coefficient is calculated from Eq 32 a, different hemoglobin gel concentrations between 5.7 % and 51.3 % have to be assumed to fit the data to Eq. 3 a.

Evaluation of the data on basis of the formula of Kozinski and Lightfoot (Eq 26) was unsuccessful because the original thesis and the article use conflicting notation (eg use the same symbol for channel height and half channel height, refer the dimensionless diffusivity to bulk or wall viscosity) but arrive at formally identical equation. In addition, the correction for variable properties was impossible to recalculate even for the examples given in the thesis. This might be because the diffusivity relationship used there could not be any choice of units or reference state be made to fit the referenced data of Keller et al.

Data of the Amicon workers (published by Blatt et al 1970 and Porter, 1972) are sometimes very well predicted by the Eqs 3 and 4 in the "gelled" region, (Blatt's Fig. 34), in others instances the prediction is low by factor 2 (Blatt's Fig. 7) when for albumin, the property data of Keller et al (1971) and Kozinski (1971) are used. As pointed out by Porter, to use the formula

$$v = k \ln \frac{c_g}{c_b} \quad (3)$$

the "gel" concentration must be determined experimentally for the equipment actually used.

Porter's Fig. 23 shows excellent agreement with the prediction - however no correction for changing bulk diffusivity is made between bulk concentrations of 0.8 to 21 %. If the diffusivity data of Keller were used, the prediction would be low by 100 %.

The data of Blatt (Fig. 36) were analyzed by Kozinsky (1971) by means of Eq. 26. The prediction is low by slightly more than half the actual flux.

4.8. Summary of concentration polarization in ultrafiltration.

In the gel polarized region Eq. 3a is often used and appears to be very useful in correlating flux data. The absolute value of flux is by no means predicted reliably. The gel concentration, that is, the value of the extrapolated zero flux, varies widely for a given substance in the experiments of different authors and in different equipment. So e.g. for bovine serum albumin, analysis of data of Baker and Strathmann (1970) yields 10 and 14 %, whereas Blatt et al (1970) give data indicating several hundred percent and Kozinski 1971 about 50 % w/w.

It seems that the mass transport coefficient is not affected by bulk solution properties. The obvious explanation - that the more or less invariant properties at wall control mass transport - is not satisfactory by itself, as the prediction using wall properties becomes far too low. Additional transport mechanisms, such as the tubular pitch proposed by Porter (Bixler, in discussion to the paper of Bixler et al, 1968 was aware of the phenomenon of "plasma skimming", movement of red cells away from the wall and its implications in ultrafiltration of whole blood) or convection currents, recently pointed out by Derzansky et al (1974) are probably in action.

The mechanism of flux limitation in ultrafiltration is still controversial. The workers of the "Amicon school" disregard osmotic pressure of macromolecular solution. Lightfoot and his associates, supported by the data on osmotic pressure of albumin

solutions, determined by Scatchard and the success of their numerical calculations, hold that osmotic pressure is of major importance. The workers of Abcor take standpoint half way between, stating that either the gel or the osmotic pressure might be present, but it is difficult to differentiate between them. (Goldsmith et al, 1971).

A physical cause of flux impairment which for obvious reason does not appear in concentration polarization discussions is plugging. It was a predominant effect in the ultrafiltration with homogenous membranes in the thirties (Ferry, 1936). Blocking of pores might occur either inside the membrane - this danger is reduced by the modern asymmetric membranes - or in the entrance of the pores. This latter effect was suspected by Beder and Gillespie, 1970, in processing of pulp with wastes.

5. MODELLING OF MASS TRANSFER IN ULTRAFILTRATION.

In this thesis, the emphasis is on understanding and characterization of the physical reality leading to the limitations on permeate flux through membrane. As the unstirred flow used in experiments is unsuitable for practical applications of ultrafiltration, the analysis will not be pursued beyond the needs of the aim of the thesis.

In the following, it will be attempted to show that a pressure gradient is established across the concentration polarization boundary layer and how its magnitude might be estimated. It is reasoned that it does not contribute significantly to the diffusion of solute. Further, it will be illustrated how the concentration - dependent diffusivity modifies the steady state concentration profile and two transient solutions relevant to unsteady state ultrafiltration will be presented.

5.1. The transport across the membrane.

It has been amply shown experimentally that transport of a pure solvent through a membrane is proportional to pressure difference across the membrane.

$$v = \frac{p_1 - p_2}{m_m} \quad (33)$$

where m_m is a reciprocal permeability or a measure of flow resistance. Kuhn, 1951 has also elegantly shown that difference in solvent chemical activity, as measured in osmotic pressure difference, is equivalent to pressure in causing solvent flow.

The change in free energy of a mole of a solvent on passing through membrane from pressure p_1 to p_2 is

$$\Delta G = \int_{p_1}^{p_2} \bar{V}_s dp = - (\bar{V}_s)_{ave} (p_1 - p_2) \quad (34)$$

When the solvent is transported at constant pressure at the same rate from a solution where its activity is a_{s1} to a solution of activity a_{s2}

$$\Delta G = \int_1^2 d\mu = \int_{a_{s1}}^{a_{s2}} d\mu^c = \mu_2^c - \mu_1^c \quad (35)$$

As the change of free energy must be the same independent of driving force, the osmotic pressure

$$\pi = \frac{\mu_2^c - \mu_1^c}{\bar{V}_s \text{ ave}} \quad (36)$$

is equivalent to the pressure difference $p_1 - p_2$ in causing transport of solvent across the membrane.

5.2. The force balance in the boundary layer

In an ultrafiltration experiment, a feed solution containing molecules which are totally rejected by the membrane may be successively replaced by pure solvent. In due time, steady state will be achieved. The rejected molecules or particles present in the boundary layer of the steady state ultrafiltration experiment described are on the average stationary with respect to the apparatus. The solvent, which is permeating through the membrane is hindered by

these particles and spends a part of its pressure energy in dissipation in this layer. It is not only the "gelled" part of the boundary layer - more exactly the part which is directly able to transfer mechanical force to its support - but even the molecules which are moving in solution in the diffusional concentration gradient that take part in the energy dissipation. The forces acting upon a stationary particle must be balanced. In this case, the forces are the gradient of chemical potential and the hydrodynamic drag force on the particle (gravitational force is neglected), Hartley and Crank, 1949.

$$\frac{d\mu_p}{dx} = F_1 \cdot N' \quad (37)$$

when F_1 , drag on one particle and N' Avogadro's number. In absence of electrical field, and at constant temperature, only pressure and concentration contribute to the potential gradient

$$\bar{V}_p \frac{dp}{dx} + \frac{d\mu_p^C}{dx} = F_1 N' \quad (38)$$

$\bar{V}_p$ partial molar volume of solute and $d\mu_p^C$ signifies variations of the concentration dependent part of the chemical potential of the solute. If friction against the walls of the apparatus is neglected, the pressure drop may be given as $\frac{dp}{dx} = F_1 N' c_p$, the sum of the forces affecting the molecules in a unit volume

$$\frac{d\mu_p^C}{dx} = \frac{dp}{dx} \left(\frac{1}{c_p} - \bar{V}_p \right) \quad (39)$$

In binary system

$$c_p d\mu_p^C + c_s d\mu_s^C = 0 \quad (40)$$

$$-\frac{d\mu_s^C}{dx} = \frac{dp}{dx} \frac{1 - c_p \bar{v}_p}{c_s} = \frac{dp}{dx} \bar{v}_s \quad (41)$$

and with the definition of osmotic pressure

$$\pi = \frac{1}{\bar{v}} (\mu_s^C - \mu_{s0}^C) \quad (42)$$

$$\frac{d\pi}{dx} = -\frac{dp}{dx} \quad (43)$$

Thus as long as the fluid drag is the only outer force affecting the molecule, the pressure drop is equal to the osmotic pressure difference between bulk and membrane surface.

At some concentration the solute will be able to support mechanically a part of the drag force. Then Eq. 38 must be modified to

$$F_{sup} + \frac{d\mu_p}{dx} \frac{1}{N'} = F_l \quad (44)$$

It is obvious that in this case, the conditions at the membrane surface are characterized by a pressure = applied pressure - pressure drop across the boundary layer and a depressed water activity, but the osmotic pressure difference between the bulk and the membrane is only some fraction of the pressure drop.

Unfortunately, no strategy for the direct measurement of the pressure drop in the boundary layer could be devised.

Summing up, the observed flow across a membrane in an ultra-filtration experiment is given by

$$v = \frac{p - \Delta p - \Delta \pi}{m_m} \quad (45)$$

According to the above

$$\Delta \pi \leq \Delta p \quad (46)$$

where p is the applied pressure, Δp the pressure drop in boundary layer and $\Delta \pi$ the osmotic difference between membrane surface and bulk.

5.3. Hydraulic and osmotic models.

An experiment utilizing a step change in pressure could cast some light on the relative magnitude of osmotic or hydraulic terms in Eq 45. Assume a steady state is achieved in an ultrafiltration experiment with driving pressure difference p_0 . The ultrafiltration velocity

$$v_0 = \frac{p_0 - \Delta p_0 - \Delta \pi_0}{m_m} \quad (47)$$

where m_m the flow resistance in membrane, $\Delta \pi_0$ the osmotic pressure difference across the membrane and Δp_0 the pressure drop across boundary layer. If pressure changes abruptly to p_1 , the initial

velocity v_1^v is given by

$$v_1^v = \frac{p_1 - \Delta p_o \frac{v_1^v}{v_o} - \Delta \pi}{m_m} \quad (48)$$

assuming that measurement can be made in time so short that no change of concentration field has yet occurred. Then the pressure drop in boundary layer is proportional to velocity and the osmotic difference is unchanged. Let us consider three cases.

- I $\Delta \pi_o \ll \Delta p_o$ hydraulic model
- II $\Delta \pi_o = \Delta p_o$ mixed model
- III $\Delta \pi_o \gg \Delta p_o$ osmotic model

Defining apparent total flow resistance M

$$M_o = \frac{p_o}{v_o^v} \quad M_1 = \frac{p_1}{v_1^v} \quad (49)$$

it may be shown from Eqs 11 to 13 that

$$\frac{M_1}{M_o} = 1 \quad (\text{hydraulic}) \quad (50a)$$

$$\frac{M_1}{M_0} = \frac{\frac{p_1}{p_0} \left(1 + \frac{m_0}{M_0}\right)}{2 \frac{p_1}{p_0} - \left(1 - \frac{m_0}{M_0}\right)} \quad (\text{mixed}) \quad (50b)$$

$$\frac{M_1}{M_0} = \frac{\frac{p_1}{p_0} \frac{m_0}{M_0}}{\frac{p_1}{p_0} - \left(1 - \frac{m_0}{M_0}\right)} \quad (\text{osmotic}) \quad (50c)$$

It will be noticed that both models with an osmotic component (II and III) suggest the possibility of zero or even negative flow on pressure decrease. This is namely what would be expected if the applied pressure is lowered below the osmotic pressure at membrane-solution interface.

Assuming the validity of Eqs 44 and 48, another rearrangement may give directly the proportion of permeate flux decrease which is due to a hydraulic pressure drop

$$\frac{\Delta p_0}{\Delta p_0 + \Delta \pi_0} = \frac{p_0 \left(\frac{p_1}{p_0} - 1\right) - m_m (v_1^v - v_0^v)}{p_0 \left(\frac{v_1^v}{v_0^v} - 1\right) - m_m (v_1^v - v_0^v)} \quad (51)$$

Apparently, a value higher than 1 has no physical meaning other than to suggest that the measurement was not fast enough to get hold of the transient. A slow measurement will also underestimate the osmotic component. To get an idea of the velocity with which

the new steady state is being achieved, it may be convenient to calculate as a very approximate measure the characteristic time $\frac{D_0}{v^2}$, based on the initial permeate flux after the pressure jump and diffusivity of the solute at infinite dilution. (see 5.7).

5.4. The mass transport equations.

Some of the usual assumptions are made: the flow is unidimensional, the effect of gravity is neglected. A binary system devoid of charge is assumed (Similarly as others, the protein - salt - water system is treated as a pseudobinary mixture of protein component p and solvent component s.) Then, in stationary coordinates

$$\frac{d\rho_p}{dt} + \frac{dn_p}{dy} = 0 \quad (52a)$$

$$\frac{d\rho_s}{dt} + \frac{dn_s}{dy} = 0 \quad (52b)$$

and their sum

$$\frac{d\rho}{dt} + \frac{d(\rho v)}{dy} = 0 \quad (52c)$$

Eq 33a becomes

$$\frac{d\rho_p}{dt} + \frac{d(\rho_p v_p^v + j_p^v)}{dy} = 0$$

when the total flow is divided into a convective and a diffusional part, based upon volume average velocity v^V , assumed constant

$$\frac{d\rho_p}{dt} + v^V \frac{d\rho_p}{dy} + \frac{d}{dy} j_p^V = 0 \quad (53)$$

assuming that the partial molar volume of protein is independent of concentration. This assumption is quite realistic in view of the fact that the partial molar volume of protein in protein crystals is almost the same as at infinite dilution (Low and Richards, 1954).

The total diffusional flux with respect to mass average velocity v is given for binary system by Bird, Stewart and Lightfoot (p. 588) as

$$j_A = -j_B = -\frac{c^2}{\rho} M_A M_B D_{AB} \left(\left(\frac{\delta \ln a_A}{\delta \ln X_A} \right)_{T,p} \nabla X_A - \frac{M_A \rho_B X_A}{\rho RT} (g_A - g_B) + \frac{M_A X_A}{RT} \left(\frac{\bar{V}_A}{M_A} - \frac{1}{\rho} \right) \nabla p + k_T \nabla \ln T \right) \quad (54)$$

To arrive at the relationship between the diffusional flux with respect to volume average velocity, j_A^V and the j_A defined above

$$n_A = j_A + \rho_A v = j_A^V + \rho_A v^V$$

$$j_A^V = j_A + \rho_A (v - v^V) = j_A + \rho_A^V - \rho_A (\rho_A \bar{V}_A v_A + \rho_B \bar{V}_B v_B)$$

$$\begin{aligned}
 &= j_A + \rho_A v - \rho_A \bar{v}_A j_A - \rho_A \bar{v}_A \rho_A v + \rho_A \bar{v}_B j_A - \rho_A \bar{v}_B \rho_B v \\
 &= j_A - \rho \bar{v}_B
 \end{aligned} \tag{55}$$

Eq 53 and 54 give

$$\begin{aligned}
 \rho_A j_A^v &= -\phi_B \left(\frac{c_A}{c_B} + 1 \right) D_{AB} \left(\frac{\delta \ln c_A}{\delta \ln \rho_A} \frac{1}{\rho_A} \frac{\delta \rho_A}{dy} \right. \\
 &\quad \left. - \frac{M_A \rho_B}{\rho RT} (g_A - g_B) + \frac{M_A}{RT} \left(\frac{\bar{v}_A}{M_A} - \frac{1}{\rho} \right) \nabla p \right) \\
 j_A^v &= \phi_B \left(\frac{c_A}{c_B} + 1 \right) D_{AB} \left(\frac{\delta \ln a_A}{\delta \ln \rho_A} \frac{\delta \rho_A}{dy} - \frac{M_A \rho_A \rho_B}{\rho RT} (g_A - g_B) \right. \\
 &\quad \left. + \frac{1}{RT} \left(\rho_A \bar{v}_A - \frac{\rho_A M_A}{\rho} \right) \nabla p \right) \tag{56}
 \end{aligned}$$

Making use of the relationship between the mutual diffusion coefficient and the measured diffusion coefficient D_{AB}^v , and assuming no body forces

$$j_A^v = -D_{AB}^v \left(\frac{d\rho_A}{dy} + \left(\rho_A \bar{v}_A - \frac{\rho_A M_A}{\rho} \right) \frac{1}{RT \frac{\delta \ln a_A}{\delta \ln \rho_A}} \right) \frac{dp}{dy} \tag{57}$$

5.5. Pressure driven diffusion.

It will be attempted to estimate the magnitude of the pressure driven diffusion term in ultrafiltration experiments with bovine serum albumin.

At steady state, the net flow of protein is zero and thus

$$j_p^V = - \rho_p \bar{v}^V \quad (58)$$

The volume average velocity $\bar{v}^V$ and mass average velocity $\bar{v}$ are coupled as

$$\bar{v}^V = \bar{v} \rho \bar{v}_s \quad (59)$$

when protein is stationary

Einstein has used a hydrodynamic approach to calculate the increase in viscosity of a solution over that of the solvent. He used data on viscosity of sucrose solution to calculate the size of sugar molecules in solution. Happel and Brenner in their treatise on low Re hydrodynamics mean that the size of the sucrose molecule is at the lower range of size where the continuum model of solvent might be used. Hydrodynamic concepts are routinely applied to macromolecules in biochemistry, e.g. in the interpretation of sedimentation velocity in ultracentrifuge via Stokes law and its corrections for non-spheric particles. Thus it should be possible to use even the hydrodynamics of porous beds for flow through concentrated solutions. Here, the relationship between volume average velocity and pressure drop will be expressed through the Carman-Kozeny equation

$$-\frac{dp}{dy} = 5 S_p^2 \eta_s \frac{\phi_p^2}{(1 - \phi_p)^3} v^v \quad (60)$$

where S_p is the specific surface of a particle here taken as the surface of a molecule. Eqs 57, 59 and 60 may be combined to yield

$$\rho_p v^v = D_p^v \frac{\delta \rho_p}{dy} - \frac{\rho_p \bar{v}_p - \frac{\rho_p}{\rho} M_p}{RT \frac{\delta \ln a_p}{\delta \ln \rho_p}} 5 S_p^2 \eta_s \frac{\phi_p^2}{(1 - \phi_p)^3} v^v \quad (61)$$

$$\rho_p v^v = \frac{D_p^v \frac{\delta \rho_p}{dy}}{1 + \frac{5 S_p^2 \eta_s}{RT \frac{\delta \ln a_p}{\delta \ln \rho_p}} \frac{\phi_p^2}{(1 - \phi_p)^3} \frac{\rho_p \bar{v}_p - \frac{\rho_p}{\rho} M_p}{\rho_p} D_p^v} \quad (61a)$$

where D_p^v is the diffusion coefficient of a protein as measured e.g. by Keller.

The term in denominator may be considered a correction to the diffusion coefficient, taking into account the pressure diffusion.

The albumin molecule is often described as a rotation ellipsoid with a axial ratio of 1:3. (Fig. 5).

The volume of a molecule is approximated as

$$\frac{\bar{v}_p \cdot M_p}{N^*} = \frac{0.734 \cdot 66 \cdot 000}{6 \cdot 10^{23}} = 8.1 \cdot 10^{-20} \text{ cm}^3 = 8.1 \cdot 10^{-26} \text{ m}^3$$

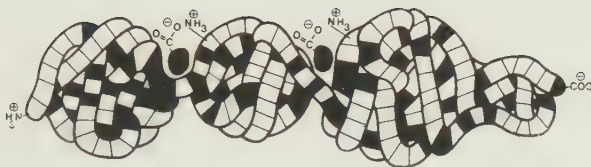


Fig. 5: Model of an albumin molecule after L.-O. Andersson, by permission of Kabi AB

Assuming for simplicity the form of cylinder terminated by half-spheres the specific area of the molecule may be calculated to

$$S_p = 1.31 \cdot 10^9 \frac{\text{m}^2}{\text{m}^3}$$

The viscosity of solvent may be taken as 10^{-3} kg/ms, $R = 8.314$ J/grad, mol.

The activity term may be evaluated from the data of Scatchard, 1946. Scatchard gives for albumin (component 2) in sodium chloride (component 3) solution

$$\frac{\delta \ln a_2}{\delta m_2} = \frac{1}{m_2} + \frac{Z_2^2}{2m_3 \left(1 - \frac{Z_2 m_2}{2m_3}\right)^2} + \beta_{22} \quad (62)$$

where m is concentration in mol/kg water and Z_2 the charge of the protein molecule.

For the case of $m_3 = 0.15$ that was investigated, β_{22} could be approximated

$$\beta_{22} = 805 - 34 Z_2 - 3.33 Z_2^2 + 122\,400 m_2 - 7000 Z_2 m_2 \quad (63)$$

If the change of volume on mixing is neglected the relationship between c_p and m_2 is given by

$$c_p = \frac{m_2}{0.001 + m_2 \bar{V}_p + m_3 \bar{V}_3} \quad (64)$$

where $\bar{V}$ is in m^3/mol . As $m_3 = 0.15$ and $\bar{V}_3 = 18 \cdot 10^{-6} \text{ m}^3/\text{mol}$ the third term in denominator is negligible compared to 0.001

$$m_2 = \frac{c_p (0.001 + m_3 \bar{V}_3)}{1 - c_p \bar{V}_p} \doteq \frac{0.001 c_p}{1 - \phi_p} = \frac{0.001 \phi_p}{\bar{V}_p (1 - \phi_p)} \quad (65)$$

$$\frac{\delta m_2}{\delta c_p} = \frac{0.001 + m_3 \bar{V}_3}{(1 - c_p \bar{V}_p)^2} \doteq \frac{0.001}{(1 - \phi_p)^2} \quad (66)$$

(Here, it was assumed that the concentration of background salt varies negligibly with protein concentration)

The activity derivative in Eq 61 may be now evaluated

$$\begin{aligned}
 \frac{\delta \ln a_p}{\delta \ln c_p} &= \frac{\delta \ln a_p}{\delta m_2} \cdot \frac{\delta m_2}{\delta c_p} c_p \\
 &= \left(\frac{1}{m_2} + \frac{Z_2^2}{0.3 \left(1 - \left(\frac{Z_2^2 m_2}{0.3} \right)^2 \right)} + 805 - 34 Z_2 - 3.33 Z_2^2 + \right. \\
 &\quad \left. + 122\,400 m_2 - 7000 Z_2 m_2 \right) \frac{0.001}{(1 - \phi_p)^2} \cdot c_p \\
 &= \frac{1 - \phi_p}{0.001 c_p (1 - \phi_p)^2} \cdot \frac{0.001 c_p}{\bar{v}_p (1 - \phi_p)} \left(1 + \frac{0.001 \phi_p}{\bar{v}_p (1 - \phi_p)} \frac{Z_2^2}{0.3 \left(1 - \frac{Z_2^2}{0.3} \right)} + \right. \\
 &\quad \left. + 805 - 34 Z_2 - 3.33 Z_2^2 + \frac{0.001 \phi_p}{\bar{v}_p (1 - \phi_p)} (122\,400 - 7000 Z_2) \right) \\
 &\quad (67)
 \end{aligned}$$

or

$$\frac{\delta \ln a_p}{\delta \ln c_p} = \frac{H}{1 - \phi_p} \quad (68)$$

where H designates the terms in paranthesis on right hand side of Eq. 67.

The correction to diffusion coefficient from Eq. 61

$$1 + \frac{D_p^v \phi_p - \frac{\rho_p}{\rho} \cdot 5 S_p^2 \eta_s \phi_p^2}{RT c_p H (1 - \phi_p)^2 \rho \bar{v}_w} \quad (69)$$

was evaluated with the numerical values given above for the full range of protein concentrations using the diffusion data of Keller et al. This data is taken in an acetic acid system at pH 4.1 whereas the activity data of Scatchard consider NaCl as the background salt. However, the correction was never found to exceed 1 % and thus in following, the pressure diffusion will be neglected.

5.6. Steady state solutions.

As shown above, at steady state (Eq. 61, the indices of D_p^v dropped hereafter)

$$v^v \frac{d\rho_p}{dy} - \frac{d}{dy} D \frac{d\rho_p}{dy} = 0 \quad (70)$$

Assuming the situation described in 5.1, the boundary conditions are

$$\begin{aligned} y = 0: \rho_p &= \rho_{pw} \\ y = \infty: \rho_p &= 0 \end{aligned} \quad (71)$$

For constant volume velocity, Eq 70 is integrated to give

$$v^v \rho_p - D \frac{d\rho_p}{dy} = 0 \quad (72)$$

and with constant D

$$\rho_p = \rho_w \exp \left(\frac{v^v y}{D} \right) \quad (73)$$

Einstein has derived the relationship

$$D \cdot \eta = k T \quad (74)$$

as well as

$$\eta = \eta_0 (1 + 2.5 \phi_p) \quad (75)$$

for the viscosity in solution of low concentration of hard spheres, where η_0 is viscosity of pure solvent and ϕ_p volume fraction of solute. Accordingly

$$D = \frac{D_0}{1 + 2.5 \phi_p} \quad (76)$$

where D_0 is diffusivity at infinite dilution

Unfortunately, the proper value of the volume fraction of protein in solution is unknown, as the protein is solvated. In addition, the solutes of interest seldom are perfect spheres.

In polymer chemistry, the concept of intrinsic viscosity $[\eta]$ is often used

$$\eta = \eta_0 (1 + 100 [\eta] \rho_p) \quad (77)$$

to avoid uncertainties of determining ϕ_p . For common spherical proteins, (Edsall, 1953) $100[\eta]$ is found to be between 3.1 and 6.2.

If from intrinsic viscosity a concentration dependent diffusivity is constructed

$$D = \frac{D_0}{1 + 100 [\eta] \rho_p} \quad (78)$$

and using it, Eq 72 integrated, the profile becomes

$$\rho_p = \frac{\rho_{pw} e^{\frac{v}{D_0} y}}{1 + 100 [\eta] \rho_{pw} \left(1 - e^{\frac{v}{D_0} y} \right)} \quad (79)$$

Happel and Brenner show that for viscosity of somewhat more concentrated solutions

$$\eta = \frac{\eta_0}{1 - 2.5 \phi_p} \quad (80)$$

is more adequate than Einsteins formula.

In what is almost certainly a coincidence, Eq 80 predicts infinite viscosity at about the solubility limit of albumin when for ϕ_p the value $\bar{v}_p \rho_p$ is used. Then, from (45)

$$D = D_0 (1 - 2.5 \bar{v}_p \rho_p) \quad (81)$$

and

$$v^v \rho_p - D_0 (1 - 2.5 \bar{v}_p \rho_p) \frac{d \rho_p}{dy} = 0 \quad (82)$$

$$\frac{v^v}{D_0} y = \ln \frac{\rho_p}{\rho_w} - 2.5 \bar{v}_p (\rho_p - \rho_w) \quad (83)$$

Diffusivity data for high concentrations are rarely measured. A notable exception is the extensive data of Keller et al on methemoglobin and serum albumin up to 30 g/100 ml and the data of Wang et al on ovalbumin up to 25 g/100 ml.

Keller et al, 1971, expressed their data by a one parameter function

$$\frac{D_0}{D} = \frac{\alpha \phi_p}{\tanh \alpha \phi_p} \quad (84)$$

A reasonable approximation to the data is however even by

$$D = D_0 e^{-\alpha' \rho_p} \quad (85)$$

which leads to

(86)

$$\frac{v_y}{D_0} = \ln \frac{\rho_p}{\rho_{pw}} - \frac{\alpha^1 (\rho_p - \rho_{pw})}{1 \cdot 1!} + \frac{\alpha^{12} (\rho_p^2 - \rho_{pw}^2)}{2 \cdot 2!} - \dots$$

In Fig. 6, the steady state concentration profiles are plotted according to Eqs 73, 79, 83 and 86. The numerical values are chosen to represent albumin and a high flux membrane, that is $D_0 = 6 \cdot 10^{-11} \text{ m}^2/\text{s}$ and velocity 10^{-4} m/s . For Eq 74, $100 [\eta] = 4.2$ according to Oncley et al, 1947, partial volume of albumin is taken as $0.734 \text{ cm}^3/\text{g}$ and the value $\alpha = 6.4 \text{ cm}^3/\text{g}$ was determined from the data of Keller et al. The wall concentration of albumin is arbitrarily set to 0.5 g/cm^3 .

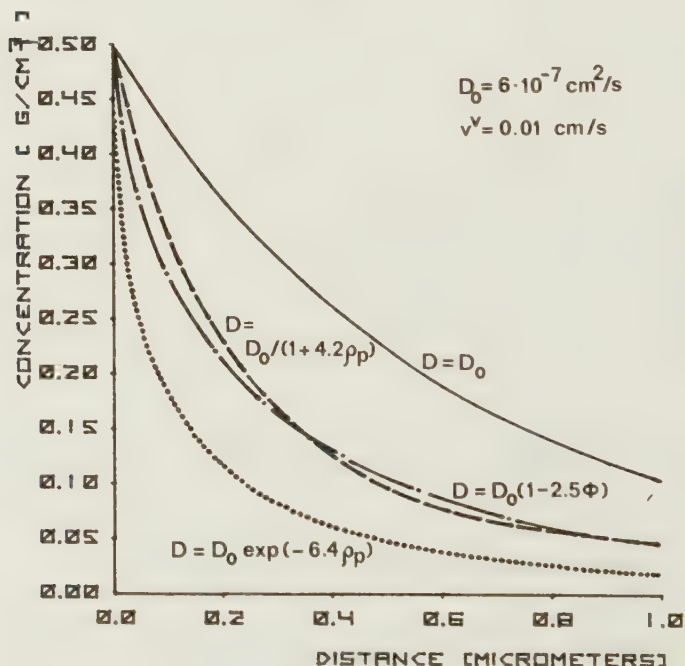


Fig. 6: Steady state concentration profiles in ultrafiltration of albumin, different diffusivity functions.

The concentration profiles reflect of course the difference in the predicted diffusivity, but the marked compression of the boundary layer compared to the constant property case should be noted. It implies namely that a steady state is reached faster and the amount of albumin in the boundary layer is less than expected.

5.7. Transient solution.

From Eq 53 several interesting facts may be derived.

Consider a transient experiment. At time zero, homogenous solution in a stagnant cell is caused to move with a constant volume velocity v^v through the cell and the membrane. The membrane rejects the solute totally. It will be assumed that the height of the cell is infinite. The appropriate initial and boundary conditions are

$$t = 0 \quad \rho_p = \rho_{p0} \quad (87)$$

$$t > 0, \quad y = 0 \quad D \frac{d\rho_p}{dy} = v^v \rho_p \quad (88)$$

Assuming constant diffusivity Eq 53 may be given as

$$\frac{\delta \rho_p}{\delta t} + v^v \frac{\delta \rho_p}{dy} - D \frac{\delta^2 \rho_p}{dy^2} = 0 \quad (89)$$

This equation is a special case of the analogous heat transfer problem treated by Carslaw and Jaeger (1959).

The Laplace transform of Eq 89 may be written down directly from Carslaw and Jaeger p.388,

$$L(\rho_p) = \frac{\rho_{po}}{p} - \frac{\frac{v}{D} \rho_{po} \exp\left(\frac{v y}{2D} - y \sqrt{\left(\frac{v}{2D}\right)^2 + \frac{p}{D}}\right)}{p \left(\sqrt{\frac{p}{D} + \left(\frac{v}{2D}\right)^2} + \frac{v}{2D}\right)} \quad (90)$$

This function may be rearranged, with the substitution $\bar{p} = p + \frac{(v)^2}{4D}$, to give

$$L(\rho_p) = \frac{\rho_{po}}{p} + \frac{\rho_{po}}{D} \exp\left(\frac{v y}{2D} - y \left(\frac{\bar{p}}{D}\right)^{1/2}\right) \left(\frac{1}{\left(\left(\frac{\bar{p}}{D}\right)^{1/2} + \frac{v}{2D}\right)} + \frac{\frac{D}{v}}{\left(\frac{\bar{p}}{D}\right)^{1/2} + \frac{v}{2D}} - \frac{\frac{D}{v}}{\left(\frac{\bar{p}}{D}\right)^{1/2} - \frac{v}{2D}} \right) \quad (91)$$

Transformation into the time domain makes use of the tabulated transforms 12 and 17 p. 494-5, op. cit. and the rule $L^{-1}(f(p+a)) = e^{-at} L^{-1}(f(p))$.

$$\begin{aligned} \frac{\rho_p}{\rho_{po}} &= 1 - \frac{v}{D} \left(\frac{Dt}{\pi}\right)^{1/2} \exp\left(-\frac{(y - v^v t)^2}{4 Dt}\right) - \frac{1}{2} \operatorname{erfc}\left(\frac{y - v^v t}{2 (Dt)^{1/2}}\right) \\ &+ \left(\frac{1}{2} + \frac{v}{2D} (y + v^v t)\right) \exp \frac{y v}{D} \operatorname{erfc}\left(\frac{y + v^v t}{2 (Dt)^{1/2}}\right) \end{aligned} \quad (92)$$

For values of the parameter $\frac{(v^v)^2 t}{D} \gg 1$, it may be shown that the concentration at membrane

$$\frac{\rho_{pw}}{\rho_{po}} = \frac{(v^v)^2 t}{D} \quad (93)$$

To be able to appreciate the significance of the solution, it was evaluated at two velocities and plotted in Figs 7 and 8 for diffusivities $16 \cdot 10^{-11} \text{ m}^2/\text{s}$ and $6 \cdot 10^{-11} \text{ m}^2/\text{s}$, corresponding to insulin monomer, molecular mass 5700 and serum albumin, molecular mass 66000. The "normalized concentration" in figures is defined as $\frac{\rho_p}{\rho}$. The velocity 10^{-4} m/s corresponds approximately to the initial velocity achieved with the CA 35 membrane at pressure of $4 \cdot 10^5 \text{ Pa}$. It is apparent that even the faster diffusing insulin reaches extremely high concentrations at the membrane in a few seconds. In reality, the time is shorter because of the significantly lower diffusivity at higher concentrations. The distance scale makes it evident that the approximation of infinite cell height is justified.

Evidently, the concentration build-up is limited and can not exceed solubility of the solute in the solvent. To obtain approximation to the approach to steady state, Eq 89 may be evaluated with a constant wall concentration

$$y = 0 \quad \rho_p = \rho_{pw} \quad (94)$$

Again from Carslaw and Jaeger the exact solution may be obtained as

$$\frac{\rho_p - \rho_{po}}{\rho_{pw} - \rho_{po}} = \frac{1}{2} \left(\operatorname{erfc} \frac{y - v^v t}{2 \sqrt{Dt}} + \exp \frac{v^v y}{D} \operatorname{erfc} \frac{y + v^v t}{2 \sqrt{Dt}} \right) \quad (95)$$

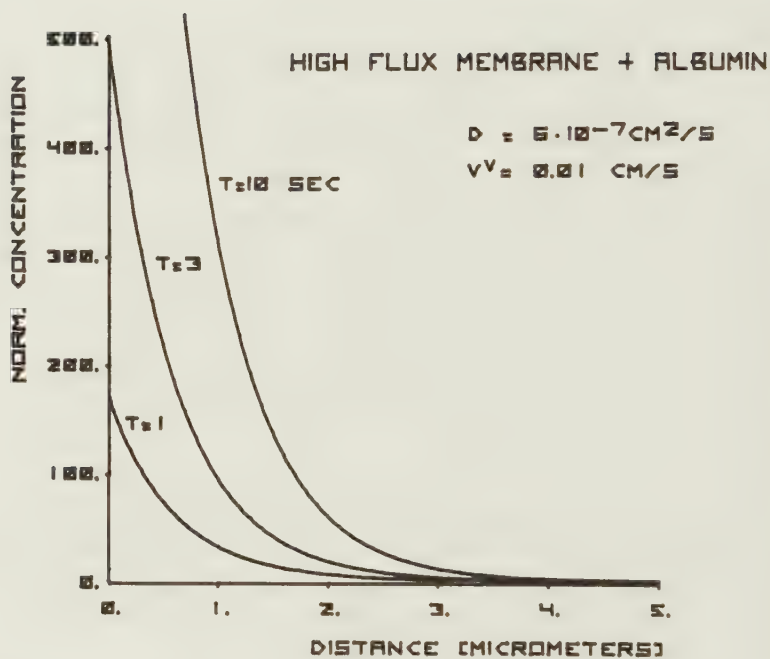


Fig. 7: Transient concentration profile in ultrafiltration of "albumin", total rejection.

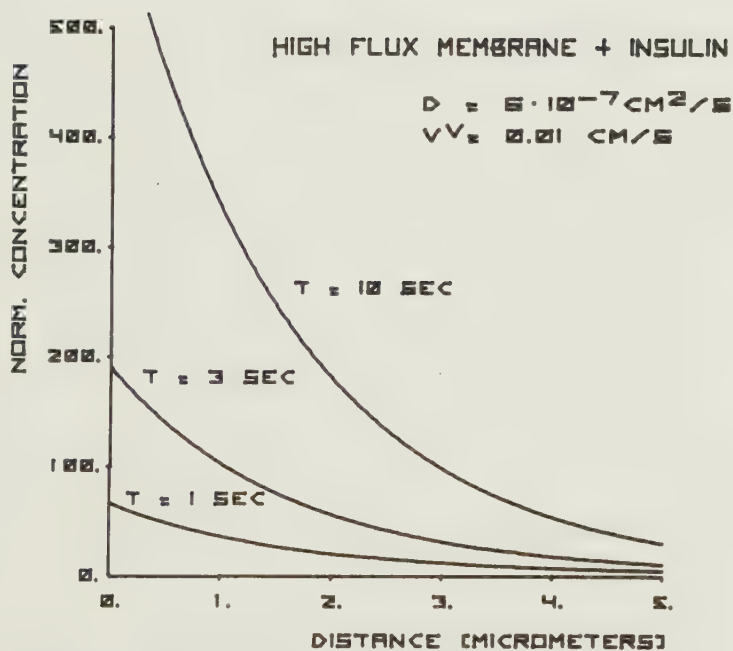


Fig. 8: Transient concentration profile in ultrafiltration of "insulin", total rejection.

This normalized concentration is evaluated as above and plotted in Figs 9 and 10. It is apparent that steady state is reached in a time period shorter than one second for the high flux membrane. An examination of the equation shows that D/v^2 is the characteristic time. In general a dimensionless time $(v^2)^2 t/D \geq 20$ is sufficient to reach the steady state profile.

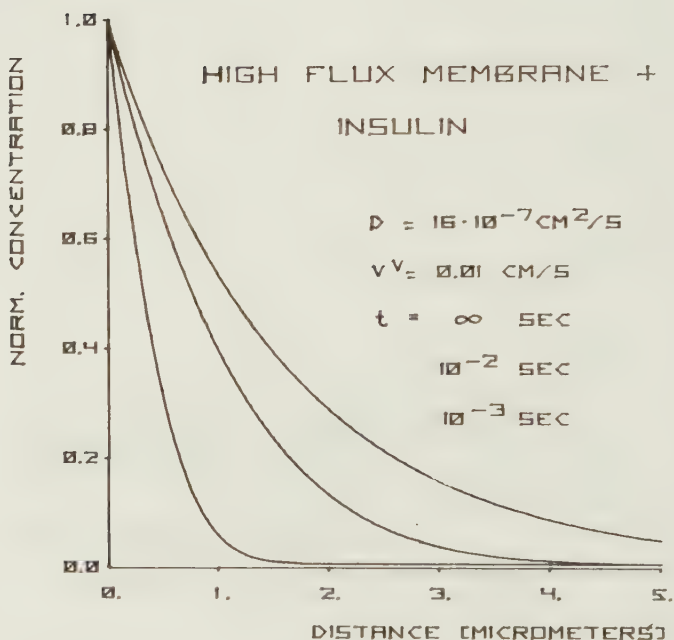


Fig. 9: Transient concentration profile in ultrafiltration of "insulin", constant wall concentration.

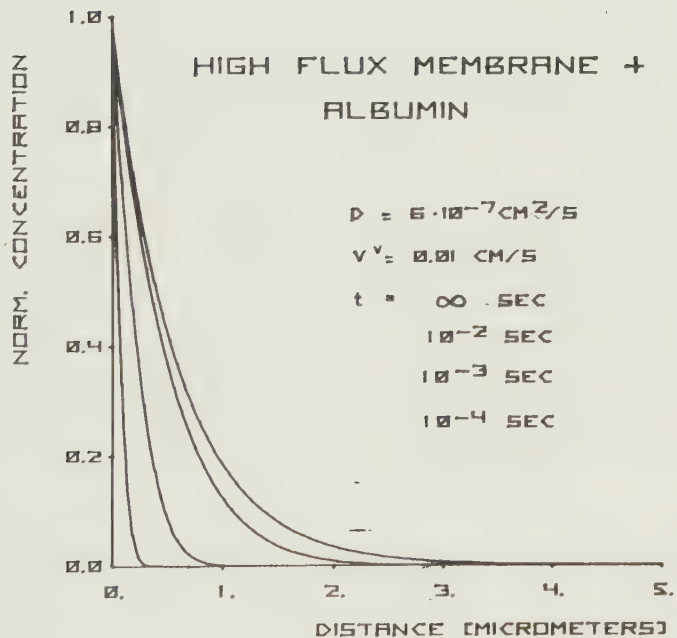


Fig. 10: Transient concentration profile in ultrafiltration of "albumin", constant wall concentration.

6. SIMPLE HYDRAULIC MODEL.

6.1. Concentration profile in the boundary layer.

It is assumed that the concentration profile in the boundary layer is similar to the one in Fig 11. It consists of a "gel" layer of approximately constant concentration ρ_{pw} and a diffusional layer of concentration varying between ρ_{pw} and the bulk concentration ρ_{pb} . The rationale beyond postulating a layer of constant concentration lies in the fact that the highest concentration a solute may reach in solution is necessarily limited.

At least for well soluble proteins, it is unlikely that there is a distinct concentration at which phase separation occurs. Bull and Breese, 1968, have observed that an amorphous glass resulted when water was removed from a concentrated protein solution. This glass developed cracks at water activities of 0.80, which corresponds to osmotic pressure of hundreds of bars, far beyond the range of practical pressures. On the other hand, there is no evidence that the concentrated solution present close to the membrane always has attributes of real gel such as shear strength.

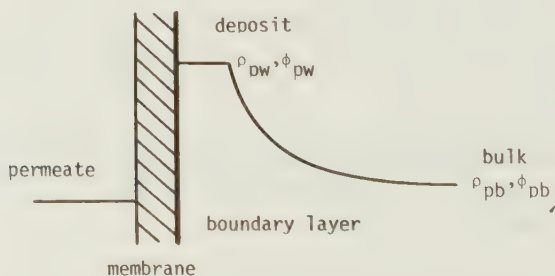


Fig. 11: Assumed concentration profile in ultrafiltration.

6.2. Sample calculations in the hydraulic model.

For a hydraulic model, Eq 45 can be reformulated

$$v^v = \frac{p}{m_m + m} \quad (96)$$

where m is hydraulic resistance of the boundary layer.

The pressure drop will be calculated from the Carman-Kozeny formula, as suggested by Blatt et al, 1970.

$$\frac{dp}{dy} = 5 S_p^2 n \frac{\phi_p^2}{(1 - \phi_p)^3} v^v \quad (97)$$

To arrive at an order of magnitude approximation to the pressure drop, albumin will be used as a model. In the albumin diffusional layer

$$\frac{d\rho_p}{dy} = \frac{v^v \rho_p}{D_0 \exp(-6.4 \rho_p)} \quad (98)$$

or in terms of ϕ_p

$$\frac{d\phi_p}{dy} = \frac{v^v \phi_p}{D_0 \exp(-8.7 \phi_p)} \quad (99)$$

The pressure drop in the diffusional layer:

From Eqs 97 and 99

$$\begin{aligned}
 \Delta p_d &= \int_{\text{diff layer}} dp = \int_0^{\phi_{pw}} 5 S_p^2 \frac{\phi_p}{(1 - \phi_p)^3} \cdot D_o \cdot \exp(-8.7 \phi_p) d\phi_p \\
 &= 5 S_p^2 \eta D_o \int_0^{\phi_{pw}} \frac{\phi_p}{(1 - \phi_p)^3} \cdot \exp(8.7 \phi_p) d\phi_p \\
 &= 5 S_p^2 \eta D_o \cdot I \quad (100)
 \end{aligned}$$

The value of the integral is shown in Fig 12. It is worth noting that the value of the pressure drop in the diffusional layer is dependent only on the maximum concentration of solute, not explicitly on flow velocity.

With the data used before and taking $\phi_p = 0.425$, the reported solubility limit,

$$\Delta p = 5 \cdot (1.31 \cdot 10^9)^2 \cdot 10^{-3} \cdot 7 \cdot 10^{-11} \cdot 0.024 = 14\,600 \frac{\text{N}}{\text{m}^2}$$

If the calculation is valid, the diffusion layer does not contribute appreciably to the pressure drop in the boundary layer.

The amount of protein in diffusional layer;

It is possible to assess the amount of protein that may be held in solution under the conditions described. Apparently the amount of protein in solution per unit surface area of the membrane,

G_{diff} ,

$$G_{diff} = \int_0^1 \rho_p dy \quad (101)$$

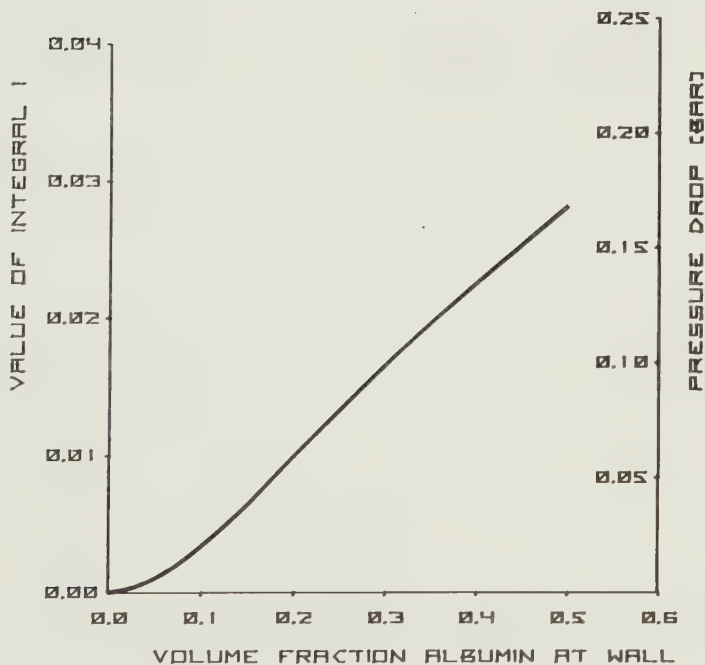


Fig. 12: Pressure drop in the diffusional layer

and combining with Eq 72

$$G_{\text{diff}} = \int_{\rho_{pw}}^{\rho_{pb}} d\rho_p = \frac{1}{v} \int_{\rho_{pw}}^{\rho_{pb}} D d\rho_p \quad (102)$$

Again using the data of Keller et al, the integral is evaluated numerically. The wall concentration is unknown but might be expected to be between 300 mg/ml and the 580 mg/ml given as the solubility by Kozinski, 1971. The diffusivity data does not reach higher than to some 300 mg/ml; however, the diffusivity can hardly increase at high concentrations and thus an upper limit on the albumin in solution may be set.

$$G_{\text{diff}} < \frac{I'}{v^V} = \frac{8.0 \cdot 10^{-9} \text{ (kg/ms)}}{v^V \text{ (m/s)}} \quad (103)$$

Pressure drop in the "gel"

The pressure drop is proportional to velocity and the thickness of the "gel" layer

$$\Delta p_g = 5 S_p^2 \eta \frac{\phi_{pw}^2}{(1 - \phi_{pw})^3} v^V \cdot \Delta l \quad (104)$$

where Δl is the thickness of the "gel" layer or

$$\Delta p_g = 5 S_p^2 \eta \frac{\phi_{pw}}{(1 - \phi_{pw})^3} v^V \cdot G_g \cdot \bar{v}_p \quad (105)$$

where G_g is the mass of solute in "gel" per unit area of the membrane. Define the specific gel resistance (m) as

$$(m) = \frac{\Delta p_g}{v^v G_g} = 5 S_p^2 \eta \frac{\phi_{pw}}{(1 - \phi_{pw})^3} \bar{v}_p [s^{-1}] \quad (106)$$

The value of specific resistance expressed in the SI units is very large, of the order of $10^{13} [1/s]$. In Fig 13, the specific gel resistance corresponding to albumin is plotted as a function of the "gel" concentration. To judge the significance of the results assume the permeate flux of $20 \text{ l/m}^2 \text{ h}$ ($\sim 12 \text{ gfd}$) and pressure drop in the gel $5 \cdot 10^5 \text{ Pa}$ (5 bar, 70 psi). The predicted amount of gel is some 9 g/m^2 , or the gel thickness $13 \text{ }\mu\text{m}$.

When the membrane is impermeable to protein the amount corresponding to the cumulated permeate γ , will be deposited as "gel" or suspended in the diffusional layer.

$$\gamma = \int_0^t v^v \rho_{po} dt \quad (107)$$

$$G_g = \gamma - G_{diff}$$

The permeate velocity will be given by

$$v^v = \frac{p}{m_m + G_g (m)} = \frac{p}{m_m + (m) \gamma - \frac{I}{v^v} (m)} \quad (108)$$

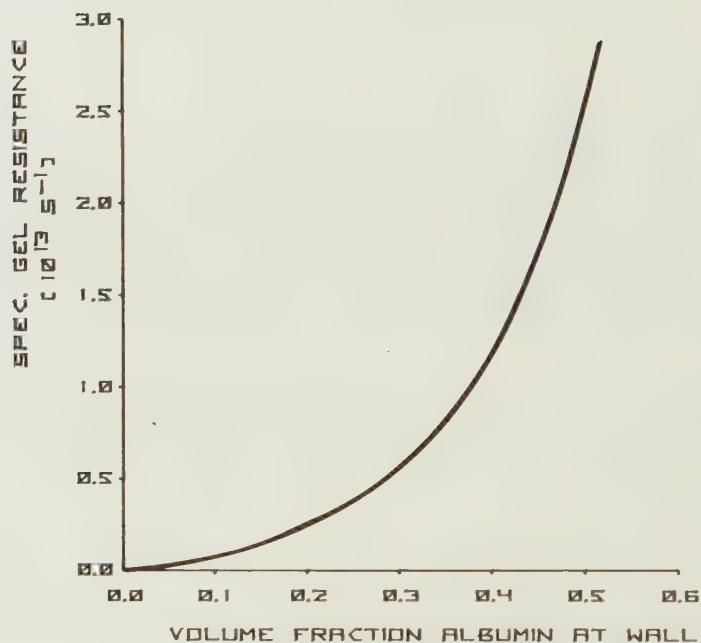


Fig. 13: Specific gel resistance according to Carman-Kozeny equation.

Eq 108 gives on rearrangement

$$\frac{1}{v^v} = \frac{m_m + (m) \gamma}{p \left(1 + \frac{I}{p}(m) \right)} \quad (109)$$

where I' is the value of integral in Eq 102 (Eq 108 seems to predict $\frac{p}{v^v} < m_m$ for $\gamma = 0$ but then $I' = 0$).

6.3. The effect of pressure

That specific "gel" resistance may be strongly pressure dependent is not unexpected. In cake filtration, it has been a well known fact that permeability of cakes is pressure dependent. It has been recognized, and experimentally confirmed, that point permeability is dependant on compressive pressure on the cake (Grace 1953 a, b, Ruth 1946, Tiller 1953, Kottwitz and Boyland 1958). It is irrelevant whether pressure is brought about by mechanical compression or the friction of the flowing liquid. In the latter case however, the compressive pressure is not uniform. It increases from zero at the surface of the cake to a value equal to pressure drop across the cake at the cake-septum interface. Designating according to Fig 14 the total applied pressure p_1 and the hydraulic pressure at the septum p_2 , in any point inside the cake the total applied pressure p_1 may be split into the sum of the hydraulic pressure p_x at that point and the compressive pressure p_{comp} , being borne by the solid particles

$$p_1 = p_x + p_{comp}$$

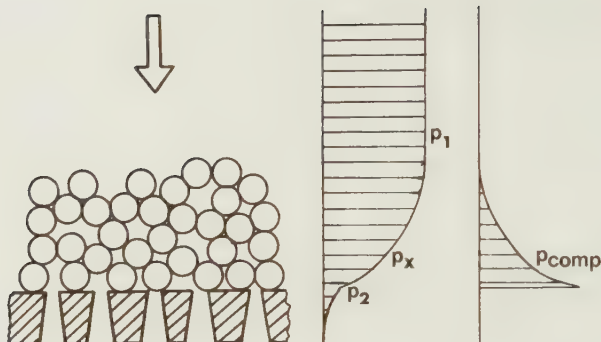


Fig. 14: Compression of the boundary layer by solvent flow.

In filtration theory, permeability of different materials is described either as specific cake resistance α (which is related to the (m) used here by $\alpha = \frac{(m)}{\eta}$) or by the parameters of some more basic flow equation, such as porosity and specific surface area in the Carman-Kozeny equation. In many cases, the specific cake resistance is adequately described by a power function of compressive pressure over 2 decades (Grace, 1953) Other workers (Tiller, 1953) prefer to correlate pressure with porosity or volume fraction of solids, e.g. $\phi_p = B p_{comp}^\beta$ with B and β empirical coefficients. Using this relationship, and noting that $dp_x = -dp_{comp}$, the Carman-Kozeny equation may be integrated for variable porosity across the cake thickness

$$\frac{dp_x}{dy} = 5 S_p^2 \eta \frac{\phi_p^2}{(1 - \phi_p)^3} v^v \quad (110)$$

or with $dy = \frac{\bar{v}_p}{\phi_p} dG_g$

$$\frac{(1 - \phi_p)^3}{\phi_p} dp_x = 5 S_p^2 \eta v^v \bar{v}_p dG_g \quad (111)$$

Integrating between the surface of the cake, with $p_x = p_1$ and $p_{comp} = 0$ and the surface of the filter media with $p_x = p_2$ and $p_{comp} = p_1 - p_2$

$$\frac{(1 - B p_{comp}^\beta)^3}{B p_{comp}^\beta} dp_{comp} = 5 S_p^2 \eta v^v \bar{v}_p G_g \quad (112)$$

The integration gives (with $\Delta p = p_1 - p_2$)

$$5 S_p^2 \eta v^v \bar{v}_p G_g = \frac{1}{B} \frac{\Delta p^{1-\beta}}{1-\beta} - 3 \Delta p + \frac{3 B}{1+\beta} \Delta p^{1+\beta} + \frac{B^2}{1+2\beta} \Delta p^{1+2\beta} \quad (113)$$

Recalling definition of (m)

$$(m) = \frac{\Delta p}{v^v G_g} = \frac{5 S_p^2 \eta \bar{v}}{\frac{\Delta p^{-\beta}}{B(1-\beta)} - 3 + \frac{3 B \Delta p^\beta}{1+\beta} - \frac{B^2 \Delta p^{2\beta}}{1+2\beta}} \quad (114)$$

It was assumed here that the specific surface area is constant. This is however often not the case in filtration. Grace's results show large increases of S_p with increasing ϕ_p (S_p calculated from the Carman-Kozeny equation). This is interpreted as effects of agglomeration. Agglomeration may cause that some of the pores do not participate in liquid flow and thus an apparently increased S_p results.

7. MATERIALS AND METHODS.

7.1. The test apparatus.

The majority of the experiments was performed in a standard, circular batch ultrafiltration cell manufactured by Amicon, with effective membrane area of approximately 25 cm^2 . The stirrer and the stirrer shaft were removed and a Cu-constantan thermocouple inserted in the solution compartment. The cell was always positioned upright, either in room temperature air or in thermostated water bath. Compressed nitrogen was used to pressurize the cell, either directly or via a stainless steel vessel of 5 l volume to replenish the cell continuously with solution. The pressure was read on a 0.5 % precision pressure gauge. The set-up is shown in Fig 5.

Concentration of solution and cell permeate were read as a rule from a UV - visible spectrophotometer, Perkin Elmer Model 402. Conductivity was measured by Kemotron Tetramatic 4 electrode conductometer. Occasionally protein nitrogen was determined by the standard Kjeldahl method.

Throughout the experiments, a number of methods for flux measurement was used. Originally a stop-watch and cylinder sufficed. Timer controlled fraction collector made later unattended operation possible. The repeability of the timer was 4 % for the shortest time setting. Finally a drop interval meter with an analog output proportional approximately to the reciprocal flux was introduced. This device (described in more detail in Appendix A), while not very accurate, made it possible to measure even the fluxes during the initial part of every experiment and the dynamic response to pressure changes. Further improvement was obtained with a recorder stepping device. Moving the recorder chart by a specific distance every time a permeate drop passed the light

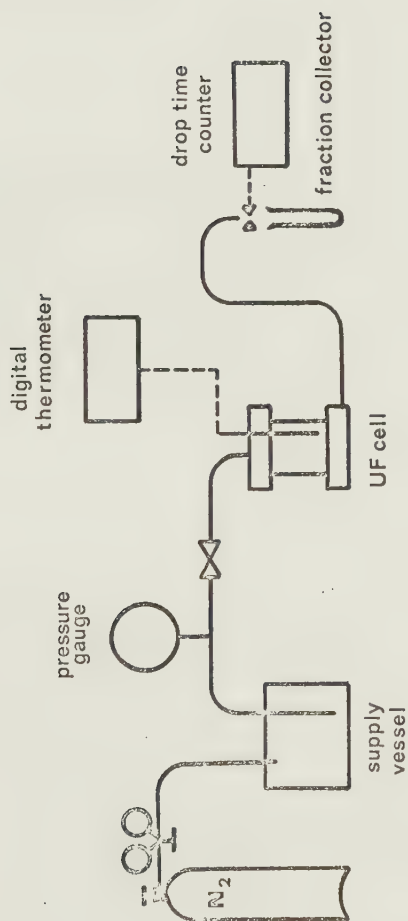


Fig. 15: The experimental set-up.

gate of the interval meter, the stepping device made the direct registration of resistance vs.deposit curve possible.

7.2. Materials

All chemicals used in the study were used as obtained, without any purification. Tap water was distilled in all glass continuous Fisons Fi-Stroom unit and deionized through Barnstead's Standard hose type cartridge. In course of the experiments it was recognized that this water contains appreciable amount of solved or suspended material (e.g. at least 2 viable organisms/ml) so that consequently water was ultrafiltrated across a protein retaining membrane before use. The designations and origins of the chemicals used are given in Table 2.

7.3. Membranes.

Predominantly cellulose acetate membranes were used. All membranes were prior to experiments rinsed in appropriate buffer or water for at least 10 minutes and run at conditions identical to the experiment to obtain a base-line permeability data. Except where indicated, each experiment was run with a virgin membrane. It was observed by others that there is no precise indication of when a membrane is satisfactorily cleaned. Even if the original permeability is restored, the cleaned membrane experiences sometimes faster flux decline than a virgin one.

The majority of experiments was performed with cellulose acetate membranes of own manufacture.

Two types of membrane, differing in permeability and retention were cast routinely in a simple continuous casting machine designed by the author. The casting dopes used were given by Van Oss and Bronson 1970. The repeatability of the membrane charac-

Table 2

Solute	Supplier
Albumin, bovine, fr.V powder	Miles Laboratories
Blue Dextran 2000	Pharmacia Fine Chemicals
Casein, after Hammarsten	Merck
Cyancobolamin	BDH Chemicals
Hemoglobin, bovine	Schuchardt
Insulin, cryst., bovine	BDH Chemicals
β -lactoglobulin	BDH Chemicals
Lysozyme from egg white, 3x crystallized	BDH Chemicals

Table 3

Designation	Flux at 10^5 Pa ($\mu\text{m/s}$)	Manufacturer
CA 50	21	in house
CA 35	6	
CA 25	2	
DDS 600	6	De Danske Sukkerfabrikker
DDS 800	4	
DDS AR 8	3-6	
DDS 870	1	
DDS 930	1.5	
DDS 975	1.5	
UM 10	14	Amicon
PM 10	60	
Iris 3042	60	Rhone-Poulenc

teristics was very satisfactory even between batches, particularly in view of the not very impressive repeatability of commercial membranes. Details of the casting machine and procedure are given in Appendix B. All membranes used are briefly characterized in Table 3.

The values of rejection given later in this paper are throughout lower than the values given by the manufacturers. The data reported here are based on unstirred experiments. It has been repeatedly observed that even mild stirring improves markedly rejection in ultrafiltration.

7.4. The experimental procedure.

The basic aim of the experiments was to find out how the macromolecular concentration polarization layer affects the transport of the solvent. Thus typically the cell was first partially filled with a macromolecular solution and then with pure solvent, taking care that the two liquids did not mix. When an amount of permeate corresponding to the amount of the original macromolecular solution had passed through the membrane the growth of the boundary layer was assumed to cease. Then, the transport of the solvent through the macromolecular deposit could be studied, under different pressures. In another type of experiment, the cell was just filled with a dilute solution and the gradual build-up of the concentration polarization layer followed by permeate flux measurement.

The actual experimental procedure varied according to whether a steady state was to be achieved or not, as well as with the price of the solutions used. 4 modes of operation resulted.

- a) growing deposit
- b) growing deposit with external supply

c) growing deposit + steady state

d) growing deposit + steady state with external supply

ad a)

The cell was loaded with an appropriate amount of solution and pressure applied directly to the cell either by bypassing the supply vessel or by having the supply vessel empty.

ad b)

The solution to be processed was placed in the supply vessel. The pressure relief valve on the ultrafiltration cell was opened and some gas admitted into the supply vessel. The solution flowed into the cell, filling it completely. When the level reached the relief valve ports, the valve was closed and the desired pressure adjusted,

ad c)

To study the steady state, the cell was filled with a given volume of a macromolecular solution and the appropriate solvent above it. To avoid mixing, a porous polypropylene disc (cut out of a material such as the disc used to support the ultrafiltration membrane in the cell) was fastened by tape in cell parallel with the membrane. Care was taken to fill the two liquids into the cell slowly and to avoid trapping air pockets under the porous partition.

ad d)

The start-up combines the features of b) and c)

In the experiments designed to reach steady state, no information is extracted from the ultrafiltration data in the region of varying concentration. The precautions described are taken only to assure a uniform boundary layer all over the membrane surface. With coloured solutions, the absence of gross mixing is readily checked. Even in the operation with external supply of the solvent, no disturbances of the sharp solution - solvent boundary were observed in carefully performed experiments.

However, in experiments run in water bath, the solution was disturbed by the bath stirrer vibrations.

8. GENERAL RESULTS.

8.1 Surface pore plugging.

Beder and Gillespie (1970) suggested that in membrane filtration of cellulose wastes the flux decline may be caused by particles blocking the entrance of the pores of the membrane, Fig 16. If it is so, one would expect that if two fouled membranes are placed face to face and run with pure water, the resistance of the sandwich would be less than the sum of the resistances of the two fouled membranes. This is because the particles blocking the pores of that membrane which is being rinsed in reverse would be dislodged (Fig 17, schematically).

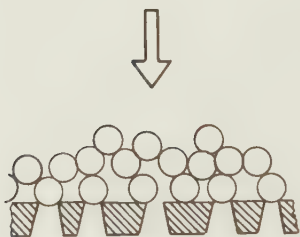


Fig. 16: Surface pore plugging

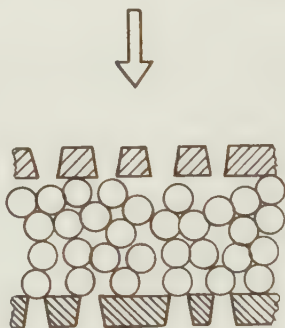


Fig. 17: Membrane sandwich - two fouled membranes face to face.

The experiments to test whether the plugging mechanism is generally valid were performed with membranes fouled by a run of at least 30 minutes, under stirring, with 0.1 % casein suspension in neutral 0.1 M tris buffer. Casein gives quite firm fouling layers which retain their characteristics to a large degree even when the fouled membranes are handled. Results of a typical experiment are shown in Fig 18. It is apparent that contrary to expectation the membrane

sandwich has flow resistance higher than the sum of the two fouled membranes. This can not be explained by increased resistance of the membrane in reverse. Two clean membranes face to face were found to give a resistance exceeding at most by 20 % the sum of the resistance of the clean membranes - a negligible increase in the situation of Fig 18. Blocking of the lower membrane by material dislodged from the upper one is not probable

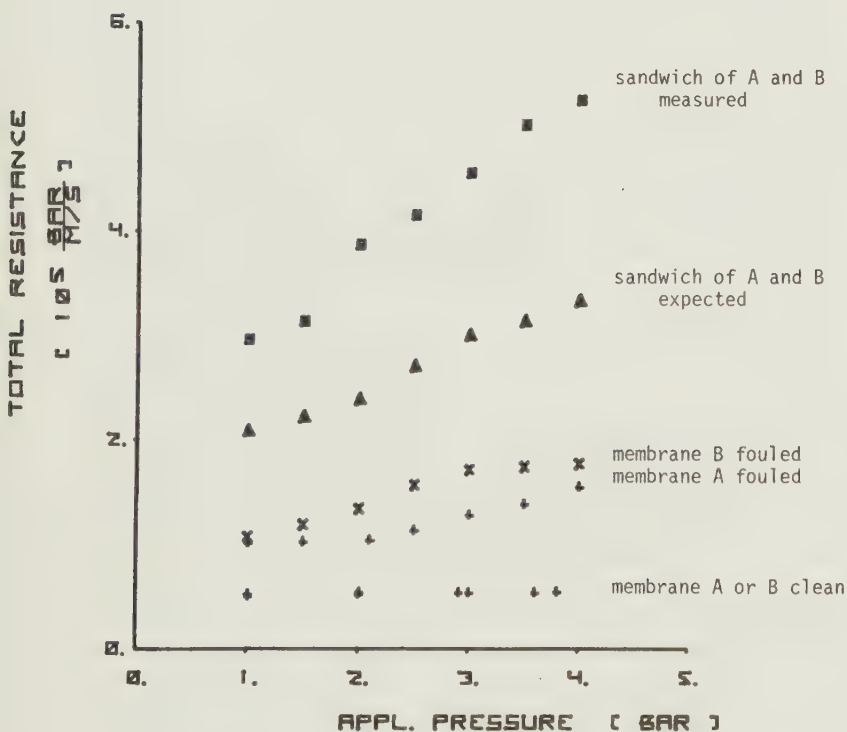


Fig. 18: Resistance to flow through a membrane sandwich.

either, as the amount of casein was found to be about $50 \mu\text{m}$ layer of anhydrous protein, definitely more than a monomolecular layer, thus there is no room for new particles on the surface of the membrane. Compression of the fouling layer by the pressure transmitted by the membrane in reverse appeared to be a likely explanation.

Unfortunately, tests with other solutes were not possible. because the fouling layer was easily disturbed or even run off during handling.

8.2. Differentiation between osmotic and hydraulic model.

There is a great deal of scatter in the data gathered according to the method proposed in chapter 5.3. The change of pressure cannot be performed momentarily and the act itself - particularly opening the relief valve to lower pressure - may disturb the solution either by chance movement or by elasticity of the membrane support material. The evaluation of the recorder strip is affected by uncertainties of the calibration curve, (see Appendix A) because small differences between large numbers are computed. Major source of scatter is the time necessary for new measurement and the size and sign of the jump.

A drop contains some 0.03 ml water and the membrane area of the ultrafiltration cell is 25 cm^2 , thus at the usual permeate flow rates, 10^{-5} m/s the time of measurement is 1s. A relevant measure of the rapidity of the measurement might be the ratio of measurement time t_{measur} and the characteristic time of the mass transfer process. With the above given data

$$\frac{t_{\text{measur}}}{D/(\bar{v})^2} = 1.2 \cdot 10^{-5} \frac{\bar{v}}{D} \quad (115)$$

For best measurement, the permeate velocity should be low. It is

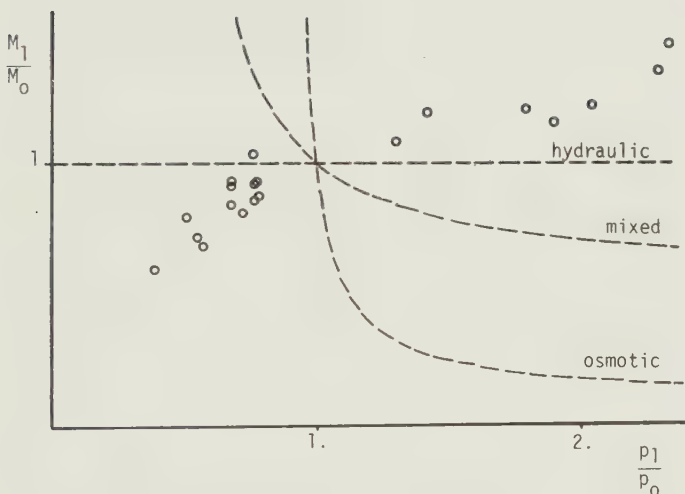


Fig. 19: Differentiating between osmotic and hydraulic models by pressure jump experiment - albumin.

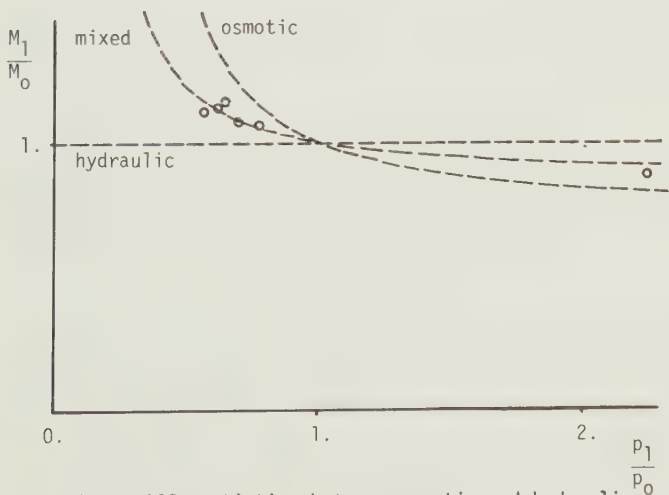


Fig. 20. Differentiating between osmotic and hydraulic models by pressure jump experiment - NaCl.

important to point out that a slow measurement, which registers a state between the true initial state and steady state, gives both Eqs 50 a, b, c and Eq 51 a bias toward the hydraulic hypothesis.

In Figs 19 and 20, experiments on albumin and common salt are evaluated according to Eqs 50 a, b, c. For Fig. 19, the full lines are drawn to correspond to ratio of $\frac{m_m}{M_0} = 0.1$. In case of salt, Fig. 20, a tighter membrane was used and the ratio is 0.7.

Two types of behaviour are seen in Figs. 19 and 20 and it seems that the osmotic model is appropriate for salt and the hydraulic for albumin. Results on other solutes will be commented upon individually in the respective chapters.

8.3. Comparison of experiments with the proposed model.

Fig. 21 is a representative copy of the tracing of the recorder coupled to drop time meter and step motor. Thus the abscissa is proportional to $\frac{1}{v}$ or $(m + m_m)$ for constant driving pressure and the ordinate to v the accumulative volume of permeate, or to γ .

The conditions of the particular experiment shown were $p = 4 \cdot 10^5$ Pa, CA 35 membrane, 2 g/l BSA in 0.15 molar NaCl, pH 7. Initial permeate velocity was $93 \cdot 10^{-6}$ m/s.

Consider e.g. the point when the permeate velocity has dropped to $3 \cdot 10^{-6}$ m/s. This point was reached after some 23 minutes, which corresponds to a dimensionless time $(v^v)^2 t / D = 210$. (Actually, it is easily shown that any point along the straight line portion of the curve would yield the same value). This value is significantly more than the 20 found to give steady state according to Eq. 94. Thus it may be concluded that the changes of permeate velocity are slow compared to the rate at which diffusional steady state is attained and quasi-steady state may be assumed.

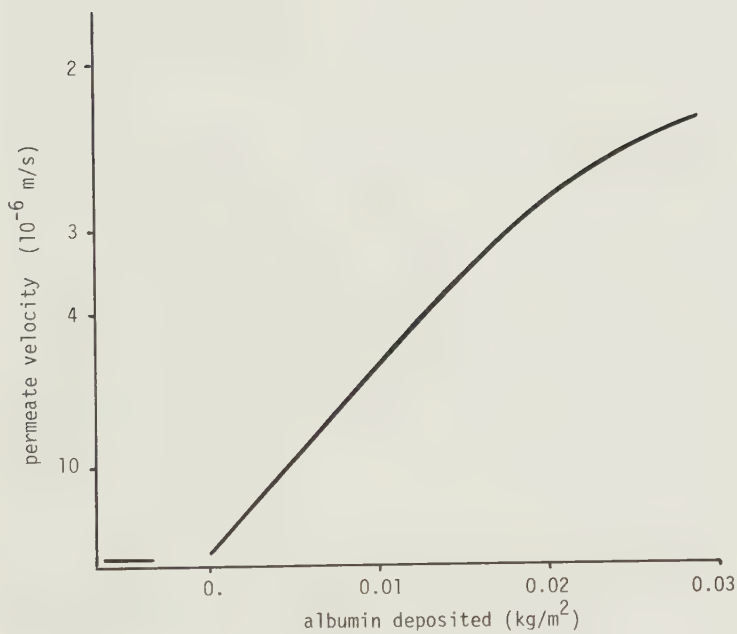


Fig. 21: Copy of recorder tracing $\frac{1}{v}$ vs. γ

At steady state, Eq. 103 predicts the maximum amount of albumin which can be held in solution by the diffusional mechanism at various permeate velocities. For $v^V = 3 \cdot 10^{-6}$ m/s, the amount is 0.0027 kg/m^2 . According to the Fig. 19 however, the permeate which passed through the membrane during the 23 minutes of the experiment must have left behind $0.017 \text{ kg albumin/m}^2$ membrane. Bearing in mind that Eq 103 overestimates albumin in solution because it does not take into account the decrease of diffusivity at concentrations higher than those measured by Keller, it appears that most of the impermeable solute left behind by permeate is deposited in the "gel" layer as indicated in Fig. 11.

According to the hydrodynamic model, Eq. 109, reciprocal of permeate velocity should be a straight line in $\frac{1}{v^V} - \gamma$ coordinates. In Fig. 19, this is true for a range of permeate velocities corresponding to $330\text{--}11 \text{ l/m}^2 \text{ h}$ ($195 - 6.5 \text{ gfd}$) which covers practically all of the range encountered in ultrafiltration and reverse osmosis. From Eq 109, and the slope of the curve in Fig. 19 the specific gel resistance (m) may be calculated. As the value of I' is not known with any certainty it will be assumed zero in all consequent calculations. The maximum error introduced by this simplification is about 15 %. With $I' = 0$, the slope of the curve leads to $(m) = 0.8 \cdot 10^{13} [\text{SI}]$. This value of specific gel resistance is obtained from the Cerman-Kozeny equation for $\phi_{pw} = 0.35$ or $\rho_{pw} = 470 \text{ mg/ml}$, see Fig. 13.

These are reasonable values. In a methemoglobin crystal, Perutz, 1962, gives the volume fraction protein as 0.45 and Matthews, 1968, in his survey of protein crystals finds values between 0.35 and 0.73.

In chapter 5.7 it was discussed that for an unsteady experiment at constant permeate velocity, the parameter $(v^V)^2 t / D$ is equal to normalized concentration at membrane. The straight line in Fig. 21 signifies that the parameter has a constant value, calculated above to be 210. From Eq. 93 it follows that $\rho_{pw} = 420 \text{ mg/ml}$ during the whole experiment, in surprising (and perhaps spurious) agreement with the value from Fig. 13.

8.4. Evidence to the compression hypothesis.

It was attempted to investigate the effect of mechanical compression on the membrane sandwich described in chapter 8.1. A porous polypropylene disc was placed on top of the upper membrane to distribute the pressure of a spiral spring. However, as the thickness of the fouling layer was of the order of micrometers, it was impossible to achieve uniform compressive pressure distribution with simple means. After a series of exploratory experiments this approach was abandoned.

Instead, the effects of pressure were deduced from the results of the unstirred cell experiments at different pressures. The simplest way of evaluation of the pressure effect is to build up the "gel" layer according to procedure c or d (layering of solution and solvent) under such conditions that the total resistance M is much higher than the resistance of the membrane m_m . Otherwise, it is necessary to apply a correction to the applied pressure p_1 to arrive to the compressive pressure Δp which affects the fouling layer

$$\Delta p = p_1 \frac{M - m_m}{M} \quad (116)$$

By varying the total amount of solute in the apparatus and consequently M or varying the resistance of the membrane m_m (using different membranes or several membranes in series) the validity of this correction was confirmed experimentally. The resulting relationship between the specific gel resistance and the compression pressure is shown for bovine serum albumin in Fig. 22. The full line drawn through the data points is a power function

$$m = 2.6 \cdot 10^{12} \Delta p^{0.72} \quad (Sl, \Delta p \text{ in bar}) \quad (117)$$

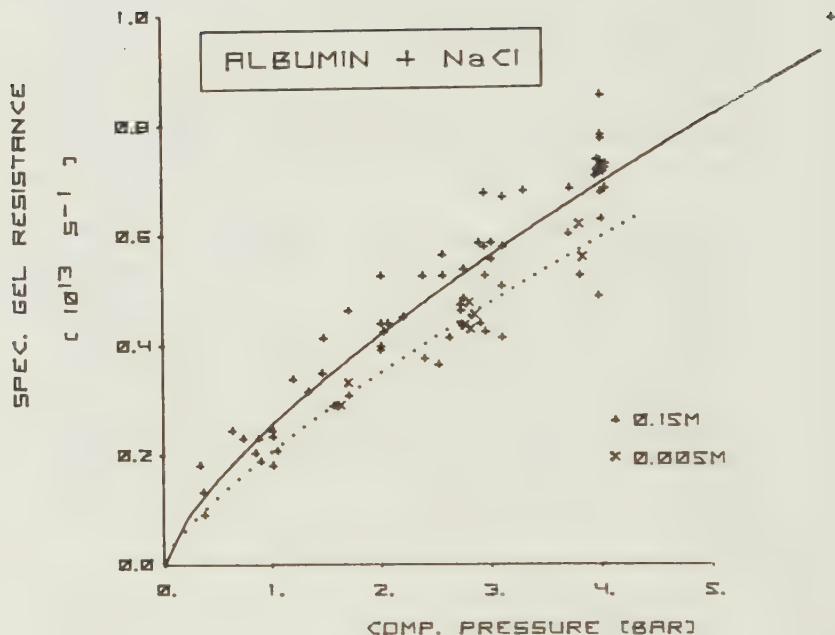


Fig. 22: Measured specific gel resistance of albumin.

In Fig 23 the corresponding relationship is plotted for Blue Dextran. It is seen that both the power function and the function derived from the porosity relationship of Tiller, Eq 114 give a good fit to the experimental data (The scatter of the dextran data is considerably less because all the data points were taken during

one run. The fit is excellent down to points taken at pressures as low as 0.05 bar).

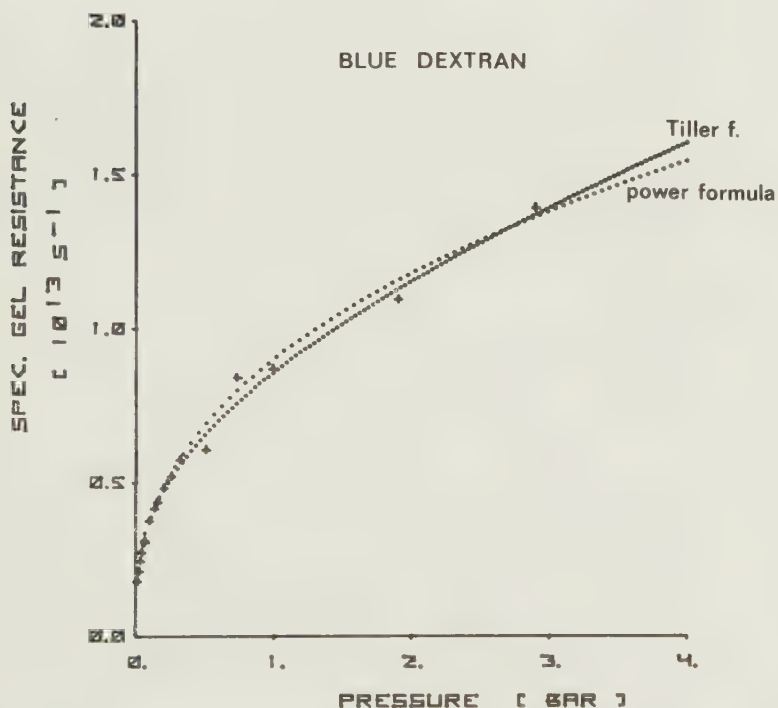


Fig. 23: Fit to measured gel resistance of Blue Dextran 2000 power law and Eq. 114.

The lag noticeable in the plot of $\frac{1}{v}$ vs. γ in experiments at low pressures, with tight membranes or low solute concentrations, is an indication of the validity of the compression hypothesis.

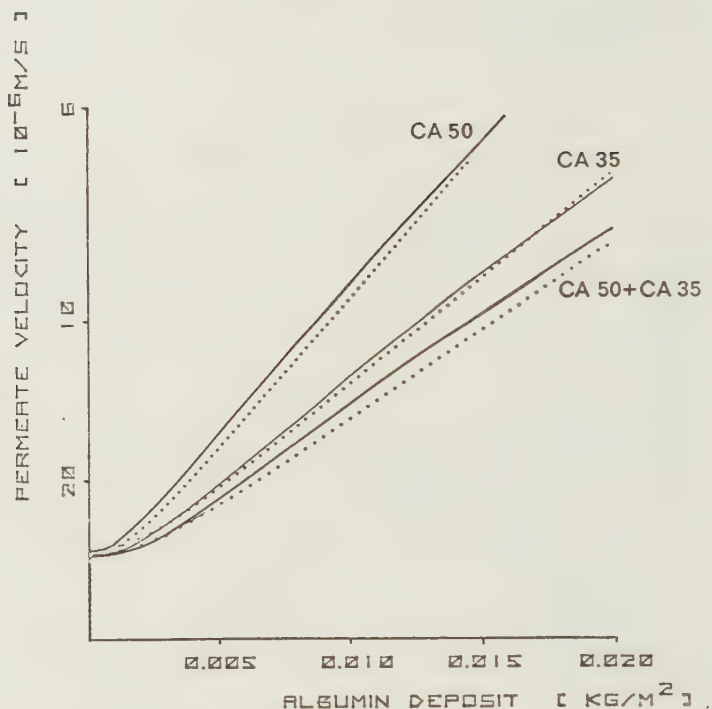


Fig. 24: Initial lag in the transient experiment.

Two membranes, CA 50 and CA 35 and a double membrane, consisting of both, were run with the same solution in such a way that the initial permeate velocities were almost the same, which means that they were run at different applied pressures. In Fig. 24, the record charts of the 3 experiments are retraced. The lag is shortest for the "fastest", most open membrane, run at the lowest pressure, and highest for the combination of two membranes. Qualitatively this is so because small amounts of deposit G_g give rise to negligible pressure drops, as the deposit is compressed only by (Eq. 116)

$$\Delta p_g = p_1 \frac{(m) G_g}{m_m + (m) G_g} \quad (118)$$

which is close to zero for large m_m . Low compressive pressure gives low (m) , see Eq. 117. When Eqs. 116 and 117 are incorporated into Eq. 108, an implicit relationship between permeate velocity and amount of deposit is obtained. (As noted before, amount of solute in the gel layer and γ are set equal)

$$v^v = \frac{p_1}{m_m + 2.6 \cdot 10^{12} G_g \left(\frac{p_1}{10^5}\right)^{0.72} \left(1 - \frac{m_m v^v}{p_1}\right)^{0.72}} \quad (118)$$

The solution is plotted with dotted lines in Fig. 24. It is seen that the power law formula describes reasonably well even the observed lag phenomenon.

The alternative explanation - diffusion seems unlikely, because Fig. 24 shows that when different membranes are run at such pressures that the initial permeate flow is identical, there are different lag periods. With equal permeate velocity, the diffusional field should be the same.

Difference in the surface of the membrane might be likewise excluded, as in the curve designated CA 35 + CA 50, the loose membrane is placed on top of the tight one, presenting the same surface to the solution as in CA 50.

8.5. The effect of temperature.

In ultrafiltration, it is common knowledge that in general increased temperature improves the permeate flux. This is of commercial

interest and the relationship between temperature and flux is often studied for specific applications (lately e.g. Kreula et al, 1974, Josefson and Munson, 1973, Grieves et al 1973, von Mylius und Saier, 1974, Donnelly and Delaney 1974). The range of temperature investigated is such that no effects on the solute are expected. Under such conditions, the permeate flux is likely to be indirectly proportional to viscosity of the solution.

According to the experiments reported here, the temperature may influence permeate flux in UF of proteins in 3 different ways, namely via

- 1) change of viscosity
- 2) in situ denaturation
- 3) denaturation prior to UF

The experiments were performed according to procedure d, with the cell immersed in water bath. Membranes were tested in advance to make sure that their resistance was not altered in the treatment. A steady state was reached in the unstirred cell, that is a concentration polarization layer in the nearest neighbourhood of the membrane and pure solvent in the rest of the cell. Then the water bath was heated. It is apparent that inevitably temperature gradients existed in the UF cell. It was not attempted to keep the heating velocity constant or the holding time at the final temperature equal. Even with the tight membrane, considerable leakage of protein occurred at high temperature. In table 4, the conditions of the experiments shown in Figures 25 to 27 are given.

Table 4.

Fig No	Solute	Amount, (mg/cm ²)	Solvent	Mem- brane	Pressure (bar)
25	albumin	1.2	0.15M NaCl	DDS 975	3
26	β lactoglobulin	1.2	0.005M NaCl	DDS 975	3
27	hemoglobin	2	0.1M phosphate	CA 50	3

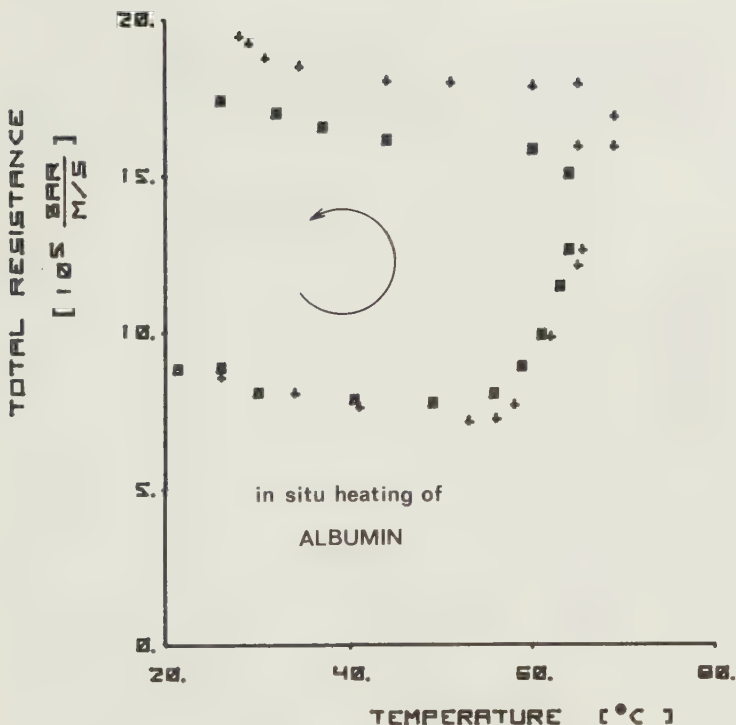


Fig. 25: In situ heating of albumin

1) change of viscosity

For all the 3 proteins studied, below 55°C the only effect observed is the effect of viscosity. In Figs 25 to 27 the total flow resistance is corrected for the appreciable changes of water viscosity and plotted against temperature. It is apparent that the lines are close to horizontal. Some additional improvement of permeate flux beyond the effect of viscosity could be hypothetically explained as follows: At increasing temperature the thermal motion of the "gel" layer is increased. Even if the time average position of the "gel" constituents is the same, the average flux is (according to the Hagen-Poiseuille equation or any other laminar

flow description) obtained by averaging in time the flow channel size to fourth power and thus flux increases with increasing amplitude of the oscillations about time-average position.

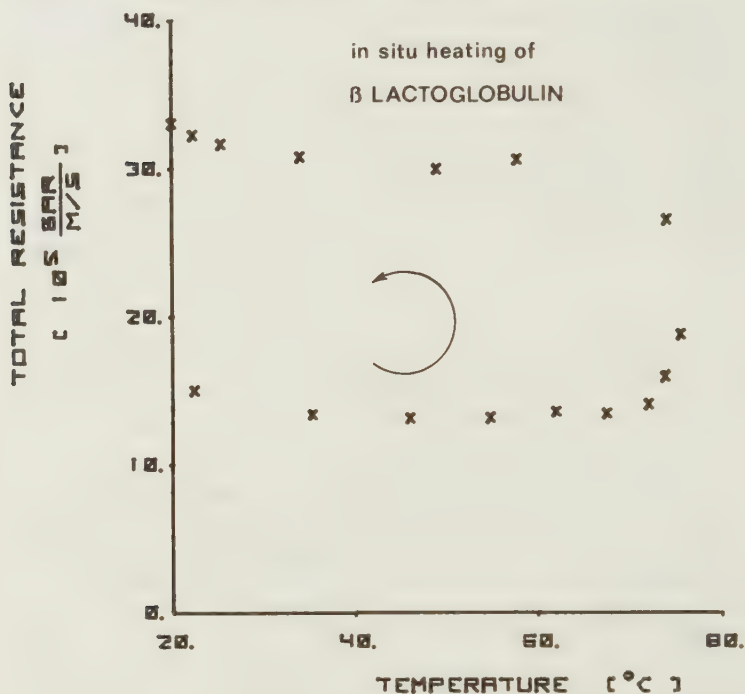


Fig. 26: In situ heating of β-lactoglobulin

2) in situ denaturation

It is a well known fact that majority of proteins experience changes of structure when they are exposed to higher temperatures in presence of water. The native structure of the polypeptide chain is unfolded and as a consequence of the exposed hydrophobic amino acid residues and eventual disulfide bond exchange reactions at higher concentrations rapid aggregation of the molecules occurs. In Figs 25, 26 and 27 a very spectacular increase of

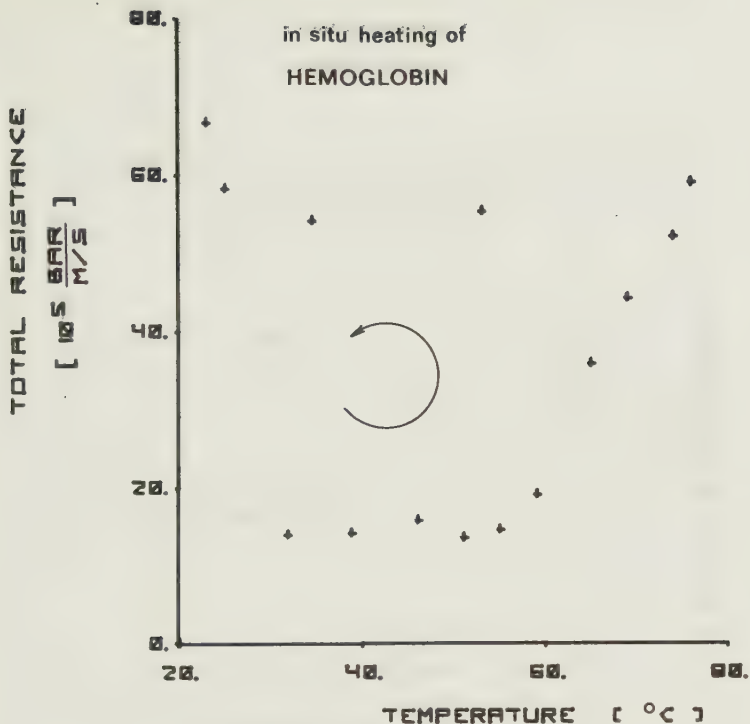


Fig. 27: In situ heating of hemoglobin

resistance is observed, at about 57°C for hemoglobin and albumin and 73°C for β -lactoglobulin. These are temperatures known to cause denaturation in these molecules. After the experiment, a continuous proteinaceous layer could be lifted off the membrane. The lack of pressure dependence of the specific gel resistance of the in situ denaturated proteins is likewise typical of a cross-linked structure, Fig. 28.

3) denaturation prior to UF

If the protein solution is heat denaturated before the ultrafiltration and ultrafiltered under non-denaturing conditions, the flow resistance is very low because the macroscopic aggregates of the denaturated protein form large flow channels in the concentration polarization layer.

In this context it is interesting to note that Muller et al 1973 report significantly increased permeate fluxes in UF of HCl and Cheddar whey after pasteurization. Higher fluxes are achieved by

more severe heat treatment. Similiar experience is noted by Pihl (1974) in UF of Herrgård cheese whey.

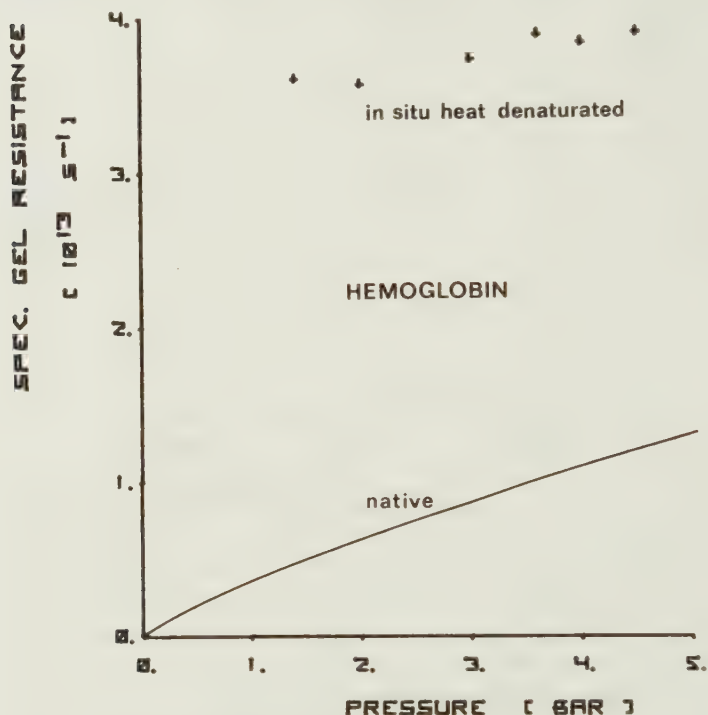


Fig. 28: Pressere dependence of the specific gel resistance of native and in situ heated hemoglobin.

8.6. Crosslinking

Glutardialdehyde is used in microscopy to fix tissues. It is a gentle crosslinking agent for proteins. Bishop and Richards, 1968, were able to crosslink crystals of β -lactoglobulin without a sensible change in the properties of the crystal.

In the experiments reported here glutardialdehyde was added to protein solutions during and after ultrafiltration runs with the

objective of fixing the structure of the boundary layer. In preliminary experiments it was found that as little as 3 % hemoglobin solution could be gelled by glutardialdehyde.

Under the osmotic hypothesis of flow limitation in ultrafiltration, one would expect crosslinking to increase permeate flow in a system containing a fixed amount of solute. Even if the osmotic pressure in concentrated solutions of macromolecules is caused not by the freedom of movement of the whole molecules but mainly by the movement of their parts (Ogston, 1966), with increasing crosslinking a decrease of osmotic pressure might be expected. In the experiments performed during steady state ultrafiltration, on addition of glutardialdehyde the resistance increased instead.

Glutardialdehyde was introduced into the cell either by switching for some time to a feed solution containing glutardialdehyde or by injecting a small amount of glutardialdehyde (< 0.1 g) into the cell. It was always attempted not to disturb the solute distribution present in the cell. Therefore, no values of the actual concentrations of glutardialdehyde in the boundary layer were available and there was no indication when the crosslinking was complete. The general picture is quite consistent. The resistance became higher with larger amounts of glutardialdehyde and longer contact times. When about 1 ml of 1 % solution were added, the increase in resistance was limited to roughly 50 %. The permeate flow through crosslinked boundary layer became proportional to the applied pressure, i.e. the resistance became constant.

It was attempted to measure the water content of the very thin crosslinked layers which could be peeled off the membrane. However the scatter of the measured values did not allow evaluation.

9. RESULTS WITH INDIVIDUAL SOLUTES.

9.1. Albumin.

Bovine plasma albumin, molecular weight 66 000 consists of a single polypeptide chain of 600 amino acid residues, heavily cross-linked by 17 disulfide bridges. It is well soluble even at its isoelectric point (pH 4,7-4,9). At pH about 4 it undergoes a conformational transition (N→F) Below pH 4, it expands considerably at low ionic strength and aggregates at higher ionic strength. (Foster 1960, Tanford 1961, del Rosario and Sun, 1973).

1) The results of ultrafiltration of albumin at low ionic strength were given in Fig. 22. There is but a small difference between the 0.15M NaCl and 0.005M NaCl solution. This suggests that concentration polarization of salt plays no role in the observed resistance - a 30 fold higher concentration polarization of the 0.005M NaCl would be needed to give essentially the same flux decrease as the 0.15M NaCl. Over a wide range of pH - 1.3 to 10 and with salt concentrations ranging from 0.15M NaCl to zero (repeated diafiltration with $15 \mu (\Omega^{-1} \text{ cm}^{-1})$ water) the specific gel resistance of albumin is quite constant. No effect is found in the pH 4 region.

2) A most spectacular decrease in permeate flow was found when albumin was ultrafiltrated at low pH (1,6-2) and high ionic strength. Figure 29 summarizes a series of experiments performed in the usual way (procedure a) under stagnant conditions in the cell at the pressure of $4 \cdot 10^5 \text{ Pa}$ (4 bar). At this pH, albumin is strongly positively charged, the repulsion forces are However screened off by the high ionic strength. The specific gel resistance increases with increasing NaCl ionic strength up to 3M, the highest NaCl ionic strength studied.

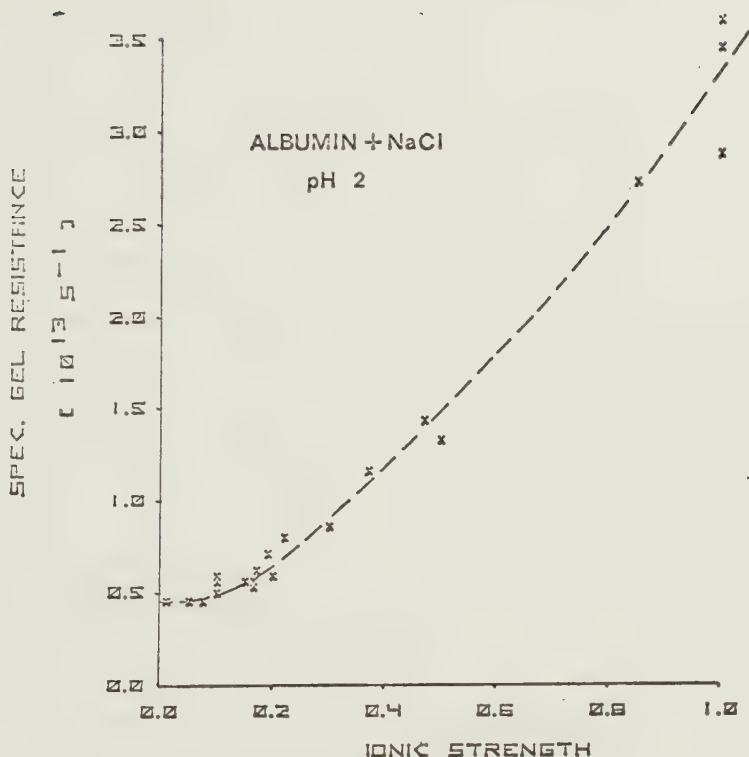


Fig. 29: Specific gel resistance of albumin at low pH and high ionic strength.

In another series of experiments, 100 cm³ 0.1 % w/w albumin solutions were ultrafiltered in a stirred cell with CA 50 membrane at $4 \cdot 10^5$ Pa (4 bar) and when steady state was reached, the permeate was returned to the cell and ionic strength adjusted. As the cell was stirred, the amount of deposit is unknown and may have varied. The ordinate of Figure 30 which describes the results is therefore reciprocal velocity rather than the gel resistance.

The effect of different salts, compared at the same ionic strength is shown. There does not appear to be a simple explanation or even a clear cut trend in the effects of the different salts. The large influence of FeCl₃ at low concentrations is notable. Other experiments show corresponding behaviour with Al (NO₃)₃.

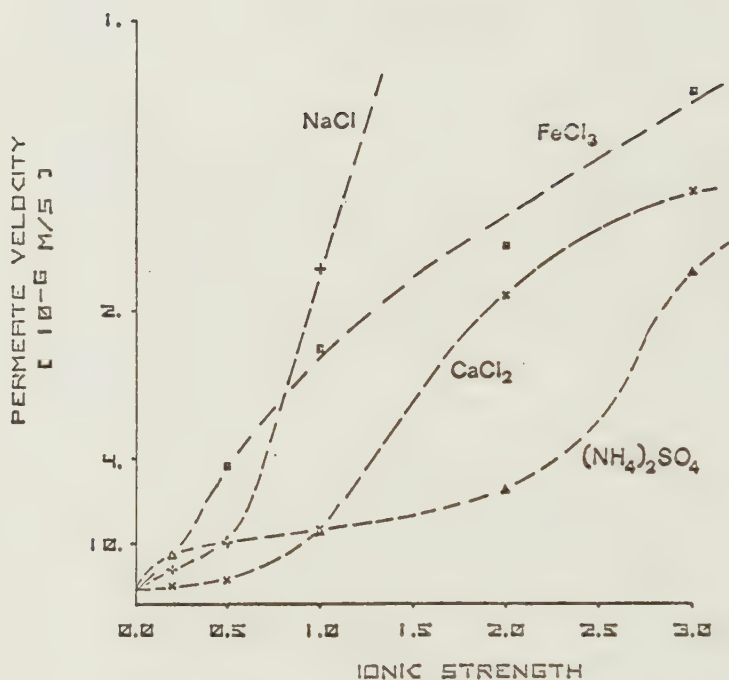


Fig. 30: Reciprocal flux of 1 g/l albumin solution in stirred cell at 4 bar, pH 2.

The results with NaCl up to 1M NaCl are fully reversible. However, addition of salt up to 3M in steps of rising concentrations gave a flux of $0.4 \cdot 10^{-6} \text{ m/s}$, while addition of salt up to 3M into distilled water resulted in a flux ten times higher.

Retention of vitamin B 12, a compact molecule of molecular weight 1000, was studied in connection with the above experiments. It appears that retention correlates quite well with resistance, Fig. 31.

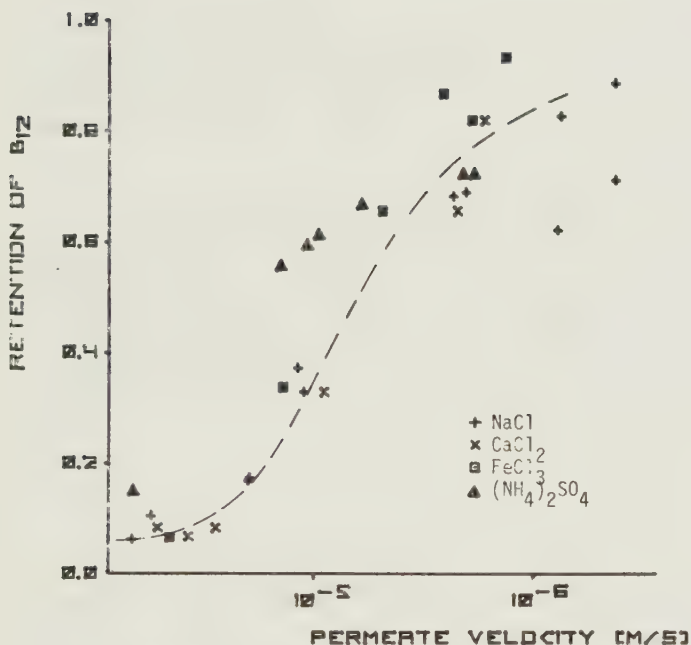


Fig. 31: Retention of vitamin B12 as a function of permeate flux of 1 g/l albumin solution at pH 2, high ionic strength.

The observed decrease in permeate flow is most easily explained by the osmotic effect of salt retention. A very moderate salt retention would be sufficient to explain the phenomenon. The charged protein layer would serve as an ion exchange membrane. Incidentally, the flux decrease at high ionic strength is negligible at pH 4.7, where the charge is low. Steady state conductivity measurements can not reveal the salt retention, because, as pointed out by Williams and Liu, 1970, for a leaky barrier the concentrations of the incoming bulk fluid and permeate are equal at steady state.

However there should be an initial reduction in permeate salt concentration, and an enrichment at the end of the experiment. The pressure jump method described earlier should show osmotic

engagement - neither of these was observed. The increasing retention of vitamin B 12 suggests that the albumin layer gets denser at higher ionic strength. If the retention were a charge dependent Donnan type phenomenon, increasing ionic strength would diminish retention.

The observed increase of resistance at pH 2 can be explained as an effect of albumin aggregation, made possible by suppression of the electrostatic repulsion by high ionic strength and by the low pH, (F) conformation which is less stable than N. Fast aggregation could also explain the above mentioned fact that 3M NaCl directly into distilled water solution gives a lower resistance than when it is added gradually, in likeness with the heat denaturation phenomena of chapter 8.5.

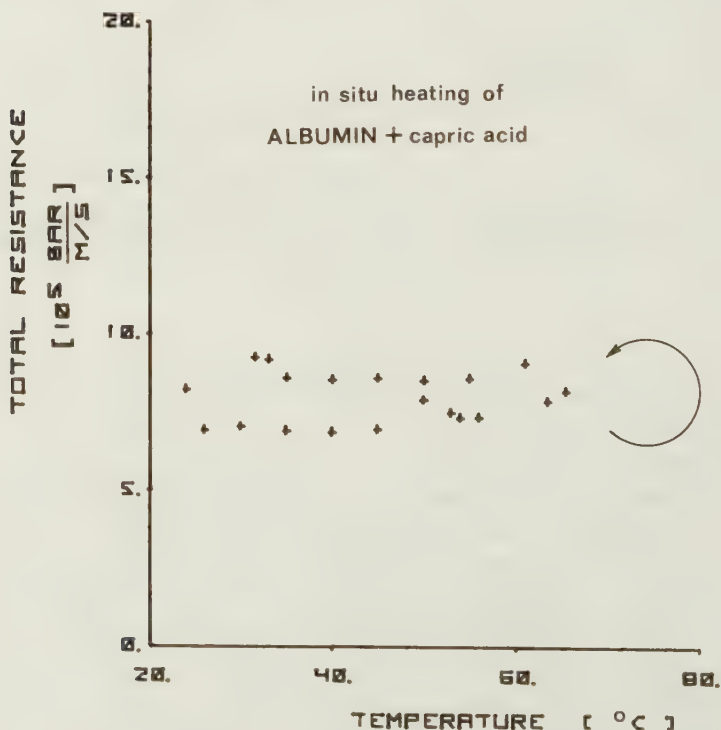


Fig. 32: In situ heating of albumin protected by capric acid.

3) The heating of albumin causes a large increase of resistance as reported in chapter 8.5.

Ever since the second world war it has been known that fatty acids protect albumin from denaturation. In Fig. 32, the effect of capric acid is apparent. Here, albumin could be heated to at least 65° without an increase of resistance, compared to about 57° in saline solution. Heating in presence of urea causes the onset of denaturation to shift toward lower temperatures, but the increase in resistance seems to be somewhat lower. The increase of resistance is much higher than usual when albumin is heated in presence of 0.1M 2-mercaptoethanol, suggesting engagement of disulfide bonds.

9.2. Hemoglobin.

Hemoglobin, the red respiratory protein of bloods has been widely studied by molecular biologists. Its molecular weight is approximately 65 000 and the hemoglobin molecule, consisting of two pairs of identical chains is almost spherical. The 4 chains are linked together by weak forces and hemoglobin is easily split into halves and even quarters by urea and other reagents competing for hydrogen bonds or by pH (below 6 and above 9.5) Hemoglobin is well soluble at physiological conditions, 0.15 ionic strength and pH 7.4. In the human red cell its concentration is 34 %.

In the experiments reported here, a commercial hemoglobin powder was used with no purification other than that a solution was always filtered prior to use. Judging by the light absorption spectrum and the reaction with KCN, the powder consisted mainly, it not entirely of methemoglobin. It dissolved slowly and not completely.

The ultrafiltration of hemoglobin in 0.15 NaCl and at neutral pH yields the typical picture encountered with other macromolecules, i.e. strong pressure dependence of the specific "gel" resistance. The behaviour in phosphate buffer is barely distinguishable from that in NaCl . (Fig. 33).

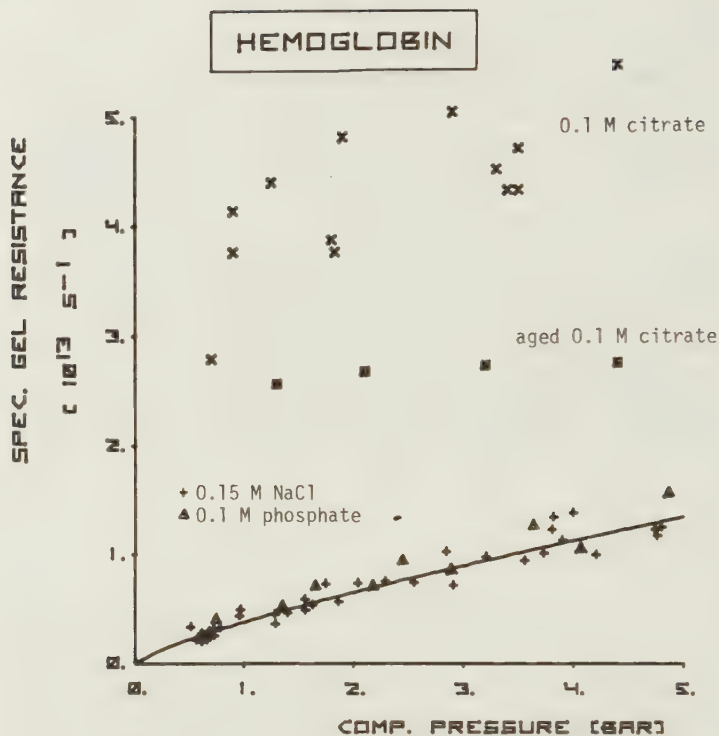


Fig. 33: Specific gel resistance of hemoglobin

A completely different behaviour is observed in citrate at pH 4.

In very low citrate concentrations, the resistance is the same as in neutral NaCl. At higher citrate concentrations the resistance is higher by an order of magnitude, Fig. 34.

This is not a simple effect of ionic strength. In Na_2SO_4 solution, which is known to salt out horse carboxyhemoglobin (Green, quoted in von H. Mippel and Schleich 1969) the increase is twofold at most, when going from 0.33 M to 1.33 M at neutral pH, see table 2 in Appendix D.

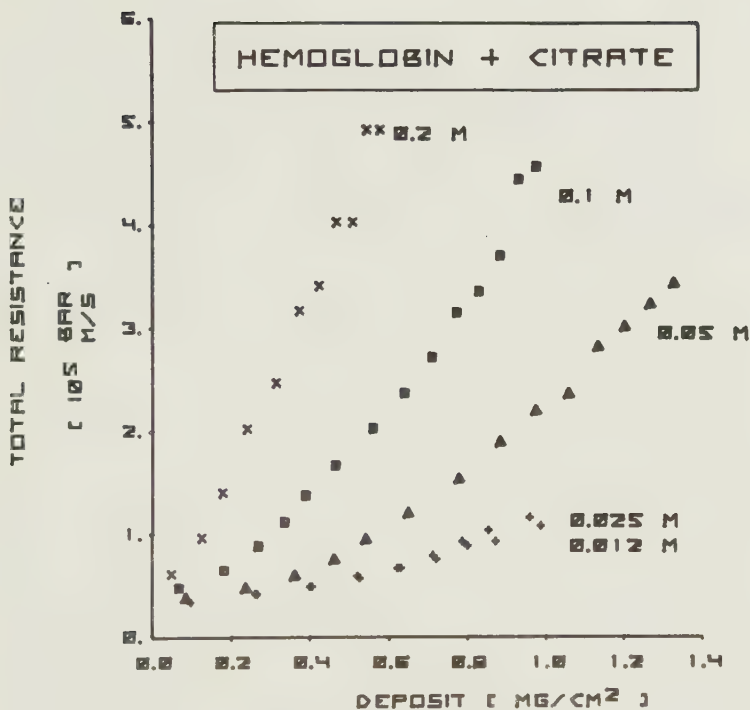


Fig. 34: Unsteady ultrafiltration of hemoglobin solutions in different citrate buffer concentrations, pH 4.

The pressure dependence of the specific gel resistance of hemoglobin in citrate is very flat as seen in Fig. 33. The deposit has the appearance of gel. This is in agreement with the fact that at pH below 4.5 hemoglobin may not only dissociate into quarter molecules but is irreversibly denaturated (Rossi Fanelli et al, 1964).

There is likely to be a specific interaction with citrate, because the same pH in 0.15M NaCl solution does not cause as much increase in resistance as the citrate. Some denaturation is observed in the saline solution at pH 4 - there is, in contrast to the neutral pH, a slow increase of resistance with time. It might be that the dramatic effect of citrate concentration actually reflects

slower kinetics of denaturation rather than different equilibria. A solution of hemoglobin in 0.1M citrate gave a significantly lower resistance when it was first kept in cold for 3 days. This is in keeping with the earlier suggestion that it is the denaturation which occurs during deposition of the protein which is responsible for the increased resistance.

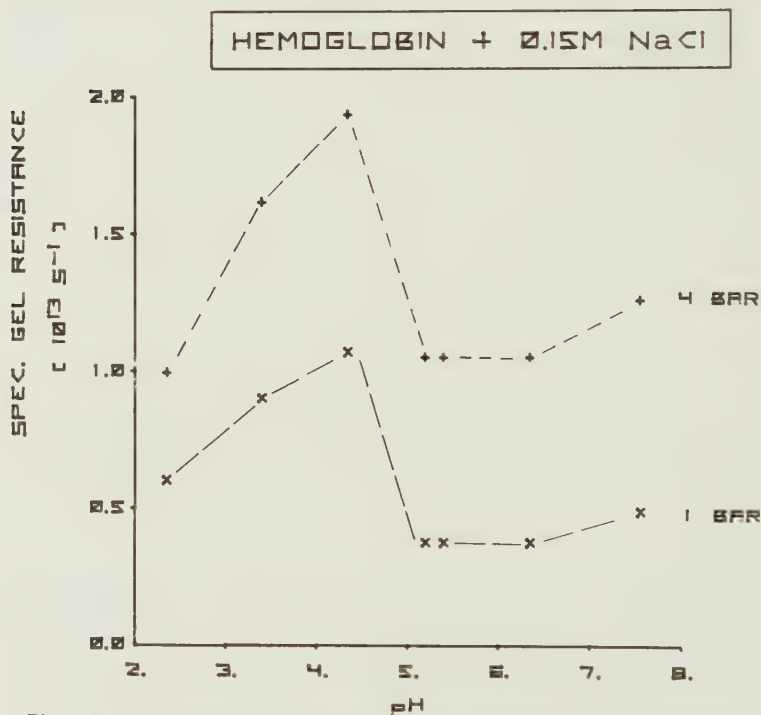


Fig. 35: Specific gel resistance of hemoglobin in 0.15 M NaCl at different pH.

Somewhat surprising is the profile of specific gel resistance with pH, Fig. 35. In 0.15 M NaCl, a maximum is observed in the region of pH 4, but at lower pH the resistance decreases again. Tentatively, this could be ascribed to the repulsion of the charged molecules.

9.3. β -lactoglobulin.

β -lactoglobulin is the major protein constituent of cheese whey. In solution it exists mainly as a dimer of 36 000 MW. The dimer is reasonably compact, with axial ratio 1:2. The isoelectric point of β -lactoglobulin is in the neighbourhood of pH 5.2. The solubility at isoelectric point is much diminished by low ionic strength of the solution, as shown in White et al, 1968.

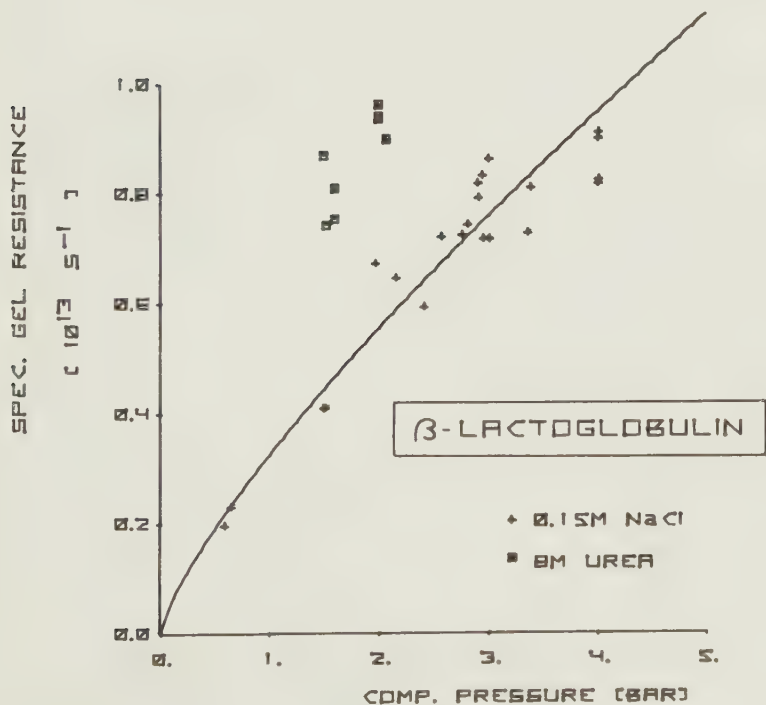


Fig. 36: Specific gel resistance of β -lactoglobulin.

The results of ultrafiltration experiments at moderate ionic strength are presented in Fig. 36. The same behaviour as with other macromolecular solutes is observed. In Fig. 37, the effects of pH on ultrafiltration of β -lactoglobulin at 4 bar compressive pressure are presented. The correlation with solubility is apparent. For the experiments in 0.15 M NaCl, no effect of pH is seen. In dilute salt solutions, the resistance is markedly increased.

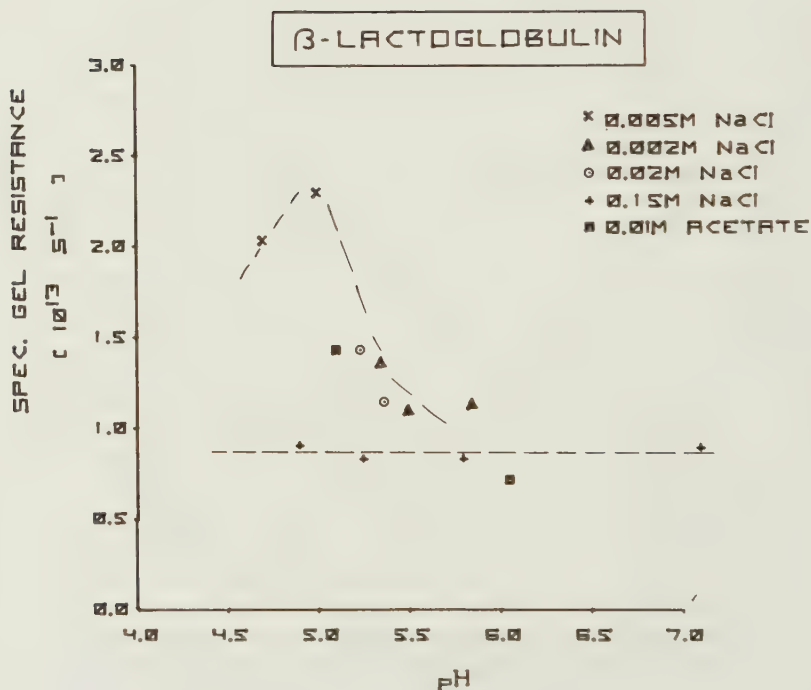


Fig. 37: Specific gel resistance of β -lactoglobulin at 4bar, effect of pH and ionic strength.

In Fig. 36, even the result of ultrafiltration of β -lactoglobulin in urea are shown. The resistance is significantly higher than for saline as solvent, in spite of the fact that the specific gel resistance was corrected by urea solution viscosity. It is likely that urea splits the dimer. The resistance data are taken during unsteady state runs of relatively short duration, about 1-2 h.

If the experiment is continued in steady state mode, the resistance continues to increase. This is in keeping with the results of McKenzie and Ralston, 1973 who found aggregation, caused by interchange of disulfide bonds in β -lactoglobulin in urea at pH 3-9.

Even in case of β -lactoglobulin it was attempted to assess the relative contribution of hydrodynamic resistance and osmotic pressure to the overall resistance. Fig. 38 suggests again that the hydrodynamic resistance dominates.

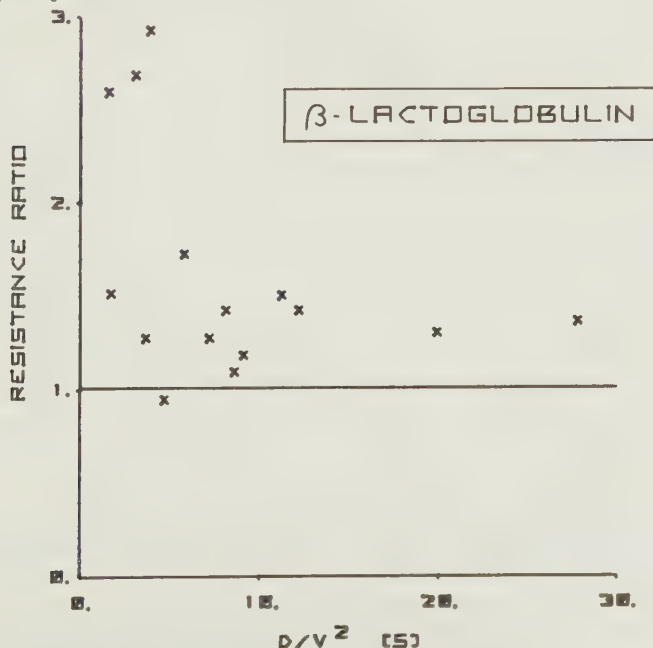


Fig. 38: Pressure jump experiment, β -lactoglobulin

9.4. Lysozyme.

The lysozyme of egg-white is a small (MW 14388) compact, roughly ellipsoidal molecule. It consists of a single peptide chain, crosslinked with 4 disulfide bridges. It is unusual between proteins by its very high isoelectric point, pH 11-11,2 (Young, 1963).

As expected, its solubility was found to be low in the region of high pH, see Appendix C.

In ultrafiltration experiments, the following observations were made.

1) As seen in Fig. 39 and Table 4 of Appendix D lysozyme's specific "gel" resistance is correlated to solubility. In neighbourhood of the isoelectric point, the specific "gel" resistance is much higher than elsewhere.

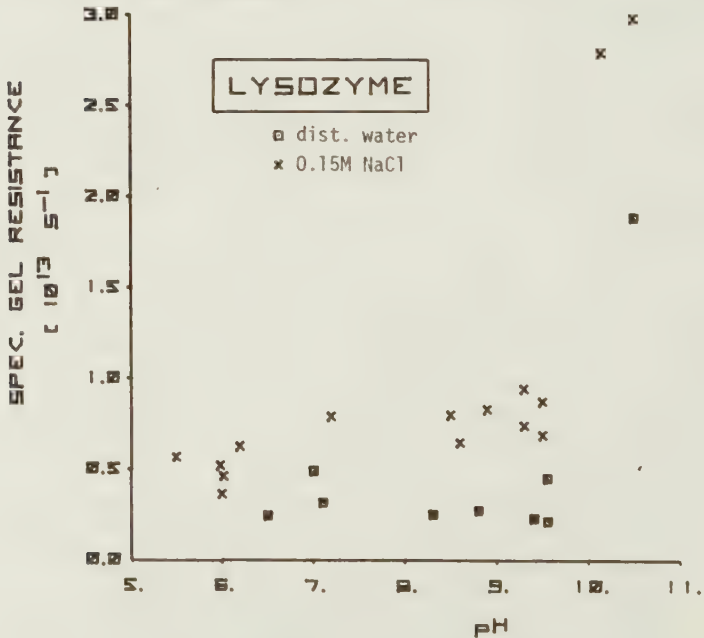


Fig. 39: Specific gel resistance of lysozyme, effect of pH and ionic strength at 4 bar compressive pressure.

2) The behaviour of lysozyme differs from the behaviour of other macromolecules investigated. At neutral pH, there is a clear difference between permeate flux of lysozyme solved in distilled water and in moderate ionic strength saline solution, (see Fig. 39), even if there is no difference in resistance of the membrane for the solvents and no detectable salt rejection.

This may be interpreted either as retention of salt in the concentrated lysozyme layer next to the membrane, causing an osmotic pressure difference or as a result of the high charge of lysozyme, which does not allow close approach of lysozyme molecules to each other in a medium of low ionic strength and thus precludes a high hydrodynamic flow resistance.

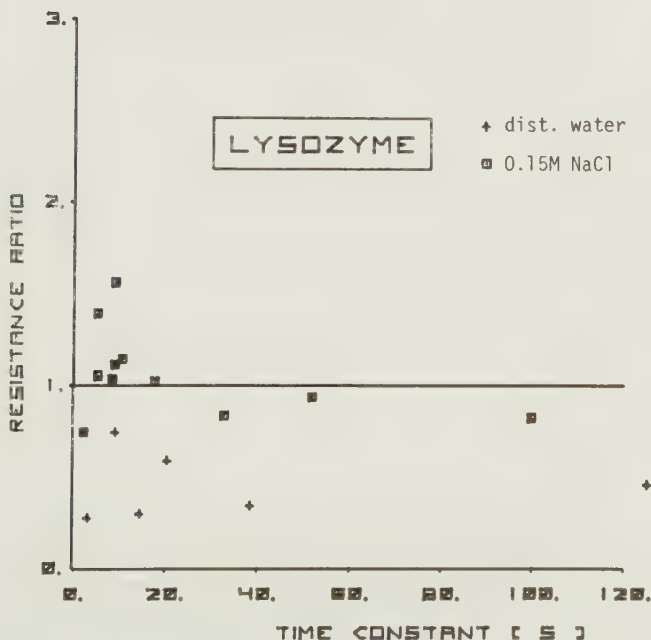


Fig. 40: Pressure jump experiment, lysozyme.

In Fig. 40 it is attempted to differentiate between the effects of osmotic pressure and flow resistance according to the pressure jump method. The osmotic involvement is apparent for both distilled water and 0.15 M NaCl even it is more pronounced for the former.

3) The pressure dependence of the specific gel resistance of lysozyme in distilled water is remarkably flat, Fig. 41, in comparison to lysozyme in salt solution Fig. 42, or other macromolecular solutes.

A flat characteristic is encountered typically where flux impairment is caused by osmotic pressure eg for salt or sugar with a slightly retentive membrane, as illustrated in Fig. 43 or for a crosslinked deposit, eg in Fig. 28.

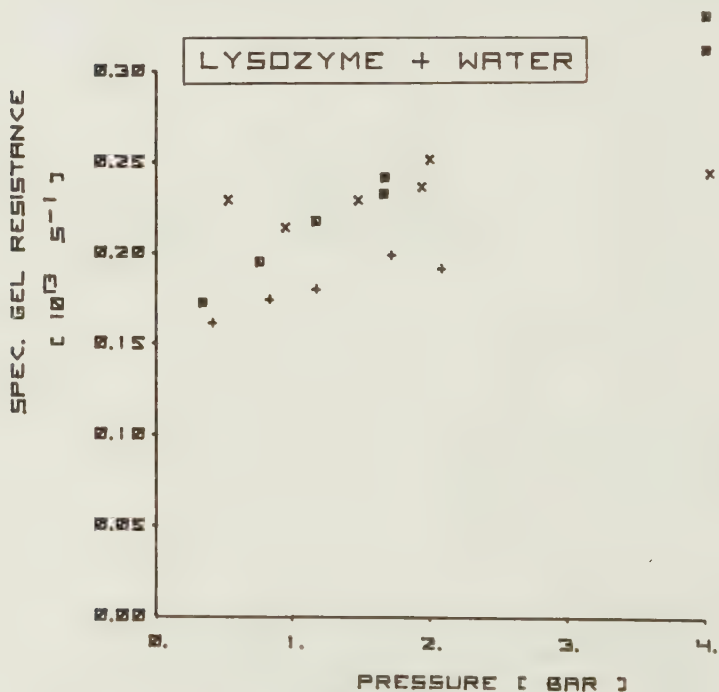


Fig. 41: Specific gel resistance of lysozyme in distilled water.

4) There is a striking difference in retention of lysozyme in distilled water and in 0.15 M NaCl. For DDS AR 8 membrane, lysozyme is retained completely in distilled water and completely passed in saline. For DDS 930, Amicon UM 10 and CA 35, the trend is the same but retention in saline is 70-80 %. The retention of lysozyme in distilled water at pH 2.2 is similar to that at neutral pH and 0.15 M NaCl.

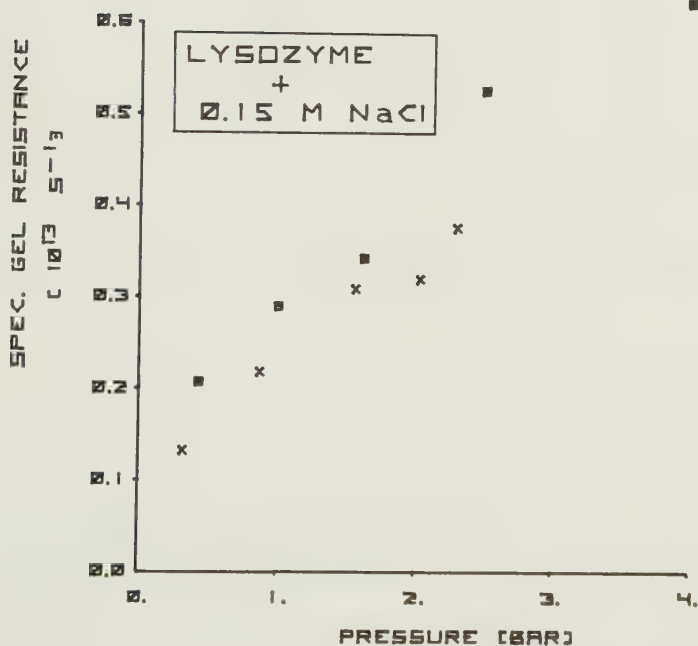


Fig. 42: Specific gel resistance of lysozyme in 0.15 M NaCl.

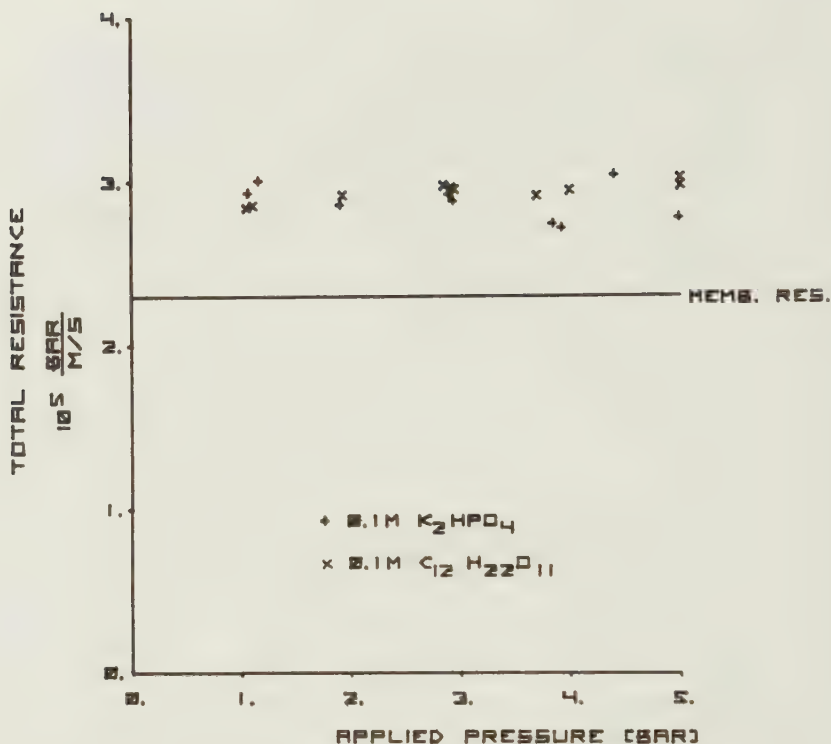


Fig. 43: Total resistance of 1 g/l solutions of phosphate and sugar, CA 25 membrane.

9.5. Other solutes.

Blue Dextran 2000.

Dextran is a polysaccharide of microbial origin. It consists of glucose residues, mostly in α -1,6 linkage. Blue Dextran 2000 is a synthetic derivative of dextran. The supplier, Pharmacia, gives its molecular weight as $2 \cdot 10^6$.

The ultrafiltration experiments with Blue Dextran are summarized in Table 5 of Appendix D and Fig. 44. The experiments show that Blue Dextran behaves in the same way as other large macromolecules tested and there are no marked difference in the ultrafiltration

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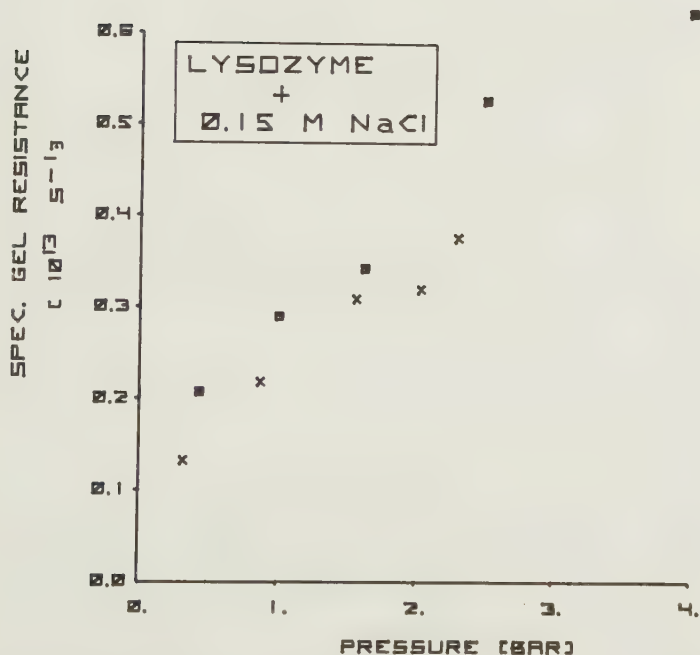


Fig. 42: Specific gel resistance of lysozyme in 0.15 M NaCl.

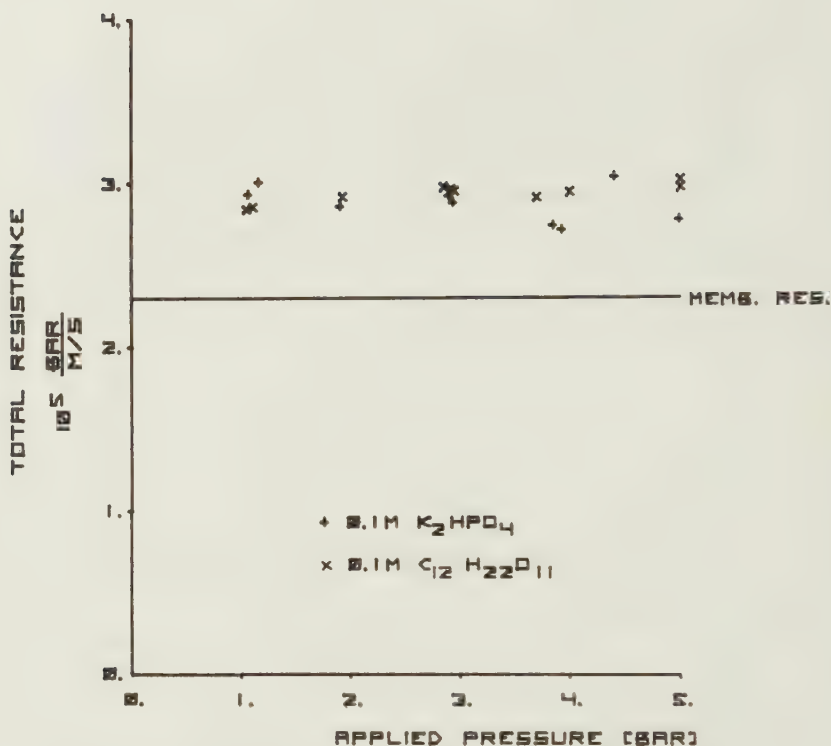


Fig. 43: Total resistance of 1 g/l solutions of phosphate and sugar, CA 25 membrane.

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The ultrafiltration experiments with Blue Dextran are summarized in Table 5 of Appendix D and Fig. 44. The experiments show that Blue Dextran behaves in the same way as other large macromolecules tested and there are no marked difference in the ultrafiltration

behaviour of Dextran in the solvents tested at low to moderate ionic strength and low to neutral pH. The specific gel resistance of Blue Dextran is much higher than that of the proteins studied.

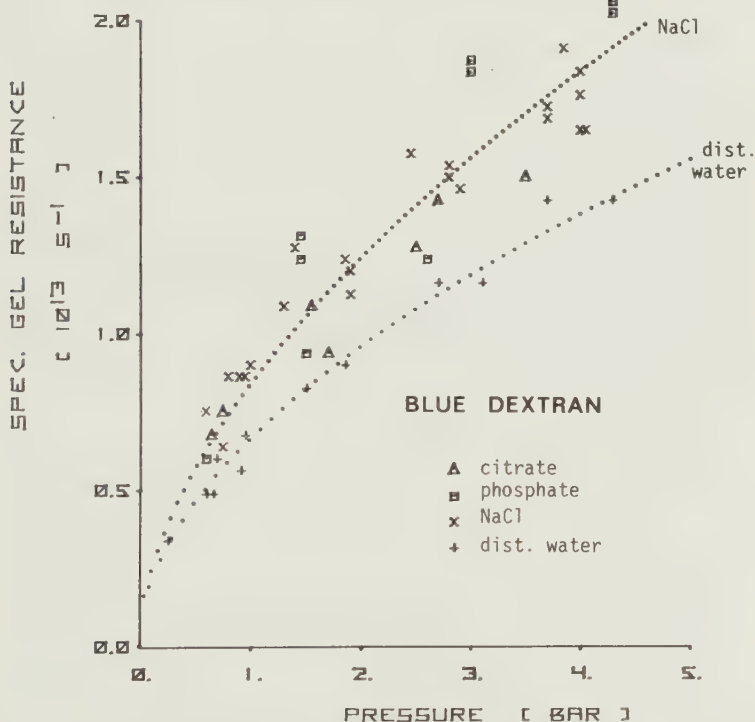


Fig. 44: Specific gel resistance, Blue Dextran 2000

Gelatin

A few measurements were performed on gelatin. At 0.6 bar compressive pressure, the specific "gel" resistance was about $0.55 \cdot 10^{13} \text{ s}^{-1}$, which is a value much higher than the resistances encountered with other proteins and about the same as for Blue Dextran 2000.

However, gelatine, which is prepared by hydrolysis of collagen has in dilute solution a configuration closer to a random coil or the expanded chains of dextran than the compact structure of the other, globular proteins considered in this study. It seems likely

that the chains of gelatin may achieve a more dense packing than the globular proteins.

Insulin

The experiments with insulin gave results difficult to interpret. The approach based on specific gel resistance seems not to be applicable. The flux decrease does not always correlate with the amount of solute present in the solution which passed the membrane and there are vast difference in the absolute values of resistance reached at different conditions. It is known (Tanford 1961, p. 236, 295) that insulin has a tendency to aggregate, even at low ionic strength (0.1) and very low pH (1.9). Higher ionic strength promotes of course aggregation.

10. CONCLUSIONS.

For the large macromolecules investigated, hemoglobin, albumin, β -lactoglobulin and Blue Dextran 2000, a relevant description of the decrease of permeate flux connected with concentration polarization can be based upon hydraulic flow resistance in the concentrated boundary layer, as proposed by the "Amicon school".

The boundary layer can be treated as consisting of a diffusional layer of varying concentration, which does not contribute to the resistance and a layer of essentially constant concentration, a "gel" layer, which causes the resistance. The "gel" layer is compressible and its resistance is dependant upon the compressive pressure applied to it. The total resistance of the boundary layer is directly proportional to the amount of deposit and to solvent viscosity. The numerical values of resistance as predicted from Carman-Kozeny equation are in reasonable agreement with experimental data.

Conditions leading to in situ aggregation of solute at the membrane lead to seriously increased resistance. This increase in resistance can be brought about by heat or by other environmental variables such as ionic strength, pH or presence of a specific chemical, e.g. citrate for hemoglobin. Trivalent ions have a pronounced effect on solubility of many macromolecules. Ultrafiltration of already denatured material at nondenaturing conditions gives less resistance.

It is suggested that the fouling observed in both reverse osmosis and ultrafiltration is to a degree caused by deposits of aggregated macromolecular solutes.

11. SYMBOLS

a	constant, Eq. 5.
a_i	chemical activity of component i
A	constant, Eq. 5
b	constant, Eq. 5
B	constant. chapter 6-3
B'	constant, Eq. 4
c	concentration, any units
c_i	concentration, mol/volume
d_h	hydraulic diameter
$\bar{D}_{ij}$	phenomenological transport coefficient in Eq. 22
D_{ij}	mutual diffusion coefficient
D_p^v	mutual diffusion coefficient of solute measured in constant volume frame of reference
D	instead of D_p^v
x_D	dimensionless diffusivity $\frac{D}{D_{\text{reference}}}$, Eq. 25
F_l	hydrodynamic drag force on one particle
F_{sup}	mechanical force acting upon a particle
g_i	body force per unit mass of component i
G	mass of solute per unit area of membrane
ΔG_i	change of molar free energy of component i
h	half channel height
H	defined by Eqs. 67 and 68
I	value of integral, Eq. 100
I'	value of integral, Eq. 102
j	diffusional mass flux with respect to mass average velocity
j^v	diffusional mass flux with respect to volume average velocity
J	diffusional molar flux with respect to mass average velocity

k	mass transport coefficient defined in Eq. 3 a.
K	constant
$\Delta \ell$	thickness of gel layer
L	length of channel
m	flow resistance in polarized layer, defined in Eq. 8
m_m	flow resistance of membrane in pure solvent
(m)	specific gel resistance, defined in Eq. 106.
m_1, m_2, m_3	component concentrations in mol/kg water
n	mass flux in stationary coordinates
N	molar flux in stationary coordinates
N'	Avogadro's number
p	pressure, applied pressure (gauge) assuming zero pressure on permeate side of the membrane
Δp	pressure drop across boundary layer
r	stirred cell radius
S_p	surface area per unit volume of solute p
t	time
u	velocity parallel to the membrane
v	mass average velocity perpendicular to the membrane
v^V	volume average velocity perpendicular to the membrane
$\vec{v}$	velocity vector
$\bar{v}$	partial volume
$\bar{V}$	partial molar volume
x	coordinate parallel to the membrane
X	mass fraction
y	coordinate perpendicular to the membrane
Z	molecular charge
α	constant, Eq. 84
α'	constant, Eq. 85
β	constant, defined in 6.3
B_{ij}	defined by Eq. 62
γ	defined by Eq. 107
$\dot{\gamma}$	shear rate

ζ	variable defined in Eq. 14
η	viscosity
x_η	dimensionless viscosity, $\frac{\eta}{\eta_{\text{reference}}}$, Eq. 25
η	intrinsic viscosity
μ	molar chemical potential
μ^C	concentration dependent part of μ
ν	kinematic viscosity
π	osmotic pressure
ρ	density
ρ_i	mass concentration of component i
ϕ	volume fraction
τ	shear stress

INDICES

A	component of a binary system
ave	average
b	bulk
B	component of a binary system
diff	diffusional layer
i	component i
g	gel layer
o	at infinite dilution, originally
p	solute, protein
perm	permeate
s	solvent
w	at wall, at membrane-solution interface

12 REFERENCES

- Agrawal, J.P., Antonson, C.R. and Rosenblatt, N.W.; "Permeability measurements of flat seawater membranes", *Desalination*, 11, 71-90, (1972).
- Alfani, F. and Drioli, E.; *Ing. Chim. It.*, 8, 235, (1972).
- Alfani, F. and Drioli, E.; "Rejection coefficient variation in the RO process", *Proceedings of the 4th int. symposium on fresh water from the sea, Heidelberg, Augusti 1973*, 4, 13, (1973).
- Astarita, G. and Greco, G.Jr.; *Chim. Ind.*, 52, 49, (1970).
- Baayens, L. and Rosen, S.L.; "Hydrodynamic resistance and flux decline in asymmetric cellulose acetate reverse osmosis membranes", *J. of Appl. Polymer Sci.*, 16, 663-670, (1972).
- Baker, R.W. and Strathmann, H.; "Ultrafiltration of macromolecular solutions with high-flux membrane", *J. appl. polym. Sci.*, 14, 1197-1244, (1970).
- Banks, W. and Sharples, A.; "The mechanism of desalination by RO and its relation to membrane structure", *OSW Res. Dev. Progr.*, 143, (June 1965).
- Bansal, B., DeLuca, R., Derzansky, L., Dewan, A.R., Doshi, M.R. and Shaw, R.A.; "Analytical and Experimental Studies of RO system", *OSW Res. Dev. Progr. Rept.*, 854, (May 1973).
- Bashow, J.D., Lawson, J.K. and Orofino, T.A.; "Hollow fiber technology for advanced waste treatment", *EPA Report No. EPA-R2-72-103*, (Dec. 1972).
- Baum, B., Margosiak, S. and Holley, W.N.Jr.; "Reverse osmosis membranes with improved compaction resistance", *Ind. Eng. Chem. Prod. Res. Develop.*, 2, 195, (1972).
- Beckman, J.E., Bevege, E.E., Cruver, J.E., Kremen, S.S. and Nusbaum, I.; "Control of fouling of RO membranes when operating on polluted surface waters", *OSW Res. Develop. Progress Rept.* 882, (Sept. 1973).
- Beder, H. and Gillespie, W.J.; "Removal of solutes from mill effluents by RO", *TAPPI*, 53, 5, 883-887, (1970).
- Bevege, E.E., Cruver, J.E., Kilbridge, J.G., Kremen, S.S. and Riedinger, A.B.; "Interaction of feed water colloids with the surface of RO membrane", *OSW Res. Develop. Progress Rept.* 883, (July, 1973).
- Bird, R.B., Stewart, W.E. and Lightfoot, E.N.; "Transport Phenomena", Wiley, New York, (1969).
- Bishop, H.K.; "Use of improved membranes in tertiary treatment by RO", *Report to EPA on WQO Program 17020 DHR Contract 14-12-417*, (Dec. 1970).

- Bishop, W.H. and Richards, F.M.; "Isoelectric point of a protein in the crosslinked crystalline state: β -lactoglobulin", *J. Mol. Biol.*, 33, 415-21, (1968).
- Bixler, H.J., Nelsen, L.M. and Bluemle, L.W.Jr.; "The development of a diafiltration system for blood purification", *Trans. Amer. Soc. Artif. Int. Organs XIV*, 99-108, (1968).
- Bixler, H.J. and Gross, R.A.; "Final report on control of concentration polarization in RO desalination of water", *OSW Res. Dev. Progr. Rept.*, 469, (Oct. 1969).
- Blatt, W.F., Dravid, A., Michaels, A.S. and Nelsen, L.; "Cake formation in membrane ultrafiltration", in *Membrane Science and Technology*, ed. J.E. Flinn, 47-97, Plenum Press.
- Breton, E.T. Jr.; "Water and ion flow through imperfect osmotic membranes", Ph. D. Thesis - University of Florida, (1958).
- Brian, P.L.T.; "Concentration polarization in RO desalination with variable flux and incomplete rejection", *Ind. Chem. Fundamentals*, 4, 439-45, (1965).
- Brown, C.E., Tulin, M.P., and Van Dyke, P.; "On the gelling of high molecular weight impermeable solutes during ultrafiltration", *Chem. Eng. Progress Symp. Series*, 67, 174-180, (1971).
- Bull, H.B., and Breese, K., 1968, reffered by Kuntz, I.D., Jr. and Kautzman, W., "Hydration of proteins and polypeptides", *Adv. Prot. Chem.*, 28, 242, (1974).
- Cantor, P.A. and Mechalias, B.J.; "Biological degradation of cellulose acetate reverse osmosis membranes", *J. Polym Sci., C*, 28, 225-241.
- Carslaw, H.S. and Jaeger, J.C., "Conduction of Heat in Solids 2nd ed., Claredon Press, Oxford 1959, 388.
- Carter, J.W., Hoyland, G. and Hasting, A.P.M., "Concentration polarization in RO flow systems under laminar conditions. Effect or surface roughness and fouling", *Chem. Eng. Sci.*, 29, 1651-1658, (1974).
- Chian, E.S.K. and Fang, H.H.P.; "Evaluation of new RO membranes for the separation of toxix compounds from water", *Water 1973, AIChE Symp. Series*, 70, 136, 497-507, (1973).
- Chi, S.W.; "Convective diffusion in axisymmetrical stagnation flow for determination of properties of membranes for RO desalination of water", *Int. J. Heat Mass Transfer*, 14, 985-988, (1971).
- Conn, W.M.; "Raw sewage reverse osmosis: Direct reclamation and phosphate removal", *Water 1971 - AIChE Symp. Series*, 68, 123, (1971).
- Copas, A.L. and Middleman, S.; "Use of convection promotion in the ultrafiltration of a gel forming solute", *Ind. Eng. Chem. Process Des. Develop.*, 13, 143-145, (1974).

- Cruver, J.E. and Nusbaum, I.; "Application of RO to wastewater treatment", Journal WPCF, 46, 2, 301, (Febr. 1974).
- Deanin, R.D., Baum, B., Margosiak, S.A. and Holley, W.H. Jr.; "Effect of Fillers on Wet Compressive Creep of Cellulose Acetate", Ind. Eng. Chem. Prod. Res. Develop., 9, 2, (1970).~
- Dejmek, P.; "Membrane Processing, report on grants 70-334/U267 and 71-1025/U822", Swedish Board of Technical Development, (Nov. 1972)(in Swedish).
- Dejmek, P., Funeteg, B., Hallström, B. and Winge. L.; "Turbulence promoters in ultrafiltration of Whey protein concentrate", J. Food Sci., 39, 1014-17, (1974).
- Dejmek, P. and Hallström, B.; "Studies of membrane deposits in ultrafiltration, in Advances in Preconcentration and Dehydration of Foods", Ed. A. Spicer, Applied Science Publ., (London 1974).
- Derzansky, L.J.; "A theoretical analysis of turbulent hyperfiltration in tubes", M. Sc. thesis, Clarkson College, (1968).
- Derzansky, L.J. and Gill, W.N.; "Mechanism of Brine-Side Mass Transfer in a horizontal Reverse Osmosis Tubular Membrane", AIChE Journal, 20, 751-60, (1974).
- Donnelly, J.K. and Delaney, R.A.; "Performance Characteristics of an Ultrafiltration Plant", Lebensm.-Wiss. u. Tehnol., 7, 3, 162, (1974).
- Doshi, M.R.; "An analysis of turbulent flow mass transfer in a rectangular duct with particular application to RO", M. Sc. thesis, Clarkson College, (1967).
- Doshi, M.R., Dewan, A.K. and Gill, W.N.; "The effect of concentration dependent viscosity on concentration polarization in RO flow systems", AIChE Symp. Ser., 68, 124, 323-339, (1971).
- Dresner, L.; "Boundary layer build-up in the demineralization of salt water by reverse osmosis", Oak Ridge Natl. Lab., Report 3621, (May 1964).
- Dresner, L.; "Concentration polarization in hyperfiltration of NaCl solution containing trace amounts of Ca^{++} and So_4^{--} ", part IV of OSW Res. Dev. Progr., REpt. 897, (Oct. 1973).
- Drioli, E., Alfani, F. and Iorio, G.; "A study on concentration polarization in RO processes", Proceedings 4th int. symposium on fresh water from the sea, Heidelberg, August 1973, 4, 115-124, (1973).
- Duval, W.A. Jr., Helfgott, T., Genetelli, E.J.; "Flux loss in RO due to dispersed organics", Water 1971 - AIChE Symp. Series 68, 250-61.
- Edsall, J.T.; "Size, shape and hydration of protein molecules," in "The Proteins", ed. H. Neuroth and K. Bailey, Vol. 1, Part B, Academic Press, New York, 1953, 692.

- Eriksson, G.; "UF processing of potato juice", in preparation (1975).
- Fenton-May, R.; "The use of reverse osmosis and ultrafiltration in the Food industry", Ph. D. Thesis, Univ. of Wisconsin, (1971).
- Ferry, J.D.; "Ultrafilter membranes and ultrafiltration", Chem. Rev., 18, 372-455, (1936).
- Feuerstein, D.L.; "RO renovation of primary sewage", Report to EPA on Project 17040 EFQ, Contract 14-12-885, (Febr. 1971).
- Fuerstein, D.L. and Burzstynski; Amer. Inst.Chem.Eng.Sympos. Series, 67 (107), 568, (1971).
- Filippi, R.P. and Goldsmith, R.L.; "Application and theory of membrane process for biological and other macromolecular solutions", in Membrane Science and Technology, ed. J.E. Flinn, Plenum Press, 33-46, (1970).
- Fisher, B.S. and Lowell, J.R.Jr.; "New technology for treatment of wastewater by RO", Report to EPA on FWQA Program 17020 DUD, Contract 14-12-553, (Sept. 1970).
- Fisher, R.E., Sherwood, T.K. and Brian, P.L.T.; M.I.T. Desalination Res. Lab., Report 295-5, (1964).
- Forbes, F.; "Considerations in the optimalization of UF", Techn. Chem. Eng., 29-34, (1972).
- Foster, J.F.; "Plasma albumin, in The Plasma Proteins", ed. F.W. Putnam, Academic Press, New York, (1960).
- Francis, P.S.; "Fabrication and evaluation of new ultrathin RO membranes", OSW Res. Dev. Progress Rept. 177, (1966).
- Gill, W.N. and Bansal, B.; "Hollow fiber reverse osmosis systems analysis and design", AIChE Journal, 19, 823, (1973).
- Gill, W.N., Derzansky, L.J. and Doshi, M.R.; "Mass transfer in laminar and turbulent hyperfiltration systems", OSW Res. Dev. Progress Rept. 403, (Febr. 1969).
- Gill, W.N., Tien, C. and Zeh, D.W.; "Concentration polarization effects in a reverse system", Ind. Eng. Chem. Fundamentals, 4, 433, (1965).
- Gill, W.N., Zeh, D.W. and Tien, C.; AIChE Journal, 12, 1141 (1966)
- Glover, F.A.; "Concentration of milk by ultrafiltration and reverse osmosis", Int. Symposium on heat and mass transfer problems in food engineering, Wageningen, (Oct. 1972).
- Glover, F.A. and Brooker, B.E.; "The structure of the deposit formed on the membrane during the concentration of milk by reverse osmosis", Journal of Dairy Res. 41, 80-93, (1974).
- Goldsmith, H. and Lolachi, H.; "Measurements of concentration polarization boundary layer in RO desalination systems", OSW Res. Dev. Progr. Rept. 727, (Dec. 1971).

- Goldsmith, R.L.; "Macromolecular ultrafiltration with microporous membranes", *Ind. Eng. Chem. Fundam.*, 10, 113-120, (1971).
- Goldsmith, R.L., de Filippi, R.P., Hossian, S., Timmins, R.S.; "Industrial ultrafiltration", in *Membrane Processes in Industry and Biomedicine*, ed. M. Bier, Plenum Press, New York-London, 267-309, (1971).
- Grace, H.P.; "Resistance and compressibility of filter cakes I and II", *Chem. Eng. Progress*, 49, 303-18, (1953 a) and 367-77, (1953 b).
- Gregor, H.P.; "Ultrafiltration membranes" proceedings of workshop symposium *Membranes in Separation Processes at Case Western University*, 174-184, (May 1973).
- Grieves, R.B., Bhattacharyya, D., Schomp, W.G. and Bewley, J.L.; "Membrane ultrafiltration of a nonionic surfactant", *AIChE Journal*, 19, 766-74, (1973).
- Gröpl, R. and Pusch, W.; "Asymmetric behaviour of cellulose acetate membranes in hyperfiltration experiments as a result of concentration polarization", *Desalination*, 8, 277-292, (1970).
- Gross, M.C., Markind, J. and Stana, R.R.; "Membrane experience in food processing", *Water 1972, AIChE Symp. Ser.*, 69, 81-88 (1972).
- Grover, J.R. and Delve, M.H.; "Operating experience with a 23 m³/day RO pilot plant", *The Chemical Engineer*, 257, 24-29, (1972).
- Happel, J., Brenner, H.; "Low Reynolds Number Hydrodynamics", Prentice-Hall, Englewood Cliffs, N.J., (1965).
- Hartley, G.S. and Crank, J.; Some fundamental definitions and concepts in diffusion processes, *Trans. Faraday Soc.* 45, 801-818, (1949).
- Hayes, J.F., Dunkerley, J.A., Muller, L.L. and Griffin, A.T.; "Studies on whey processing by ultrafiltration, 11. Improving permeation rates by preventing fouling", *Aust. J. Dairy Technol.*, 29, 132-140, (1974).
- Hendricks, T.J. and Williams, F.A.; "Diffusion layer structure in RO channel flow", *Desalination*, 9, 155-180, (1971).
- von Hippel, P.H. and Schleich, T.; "The effect of neutral salts on macromolecules, in *Structure and Stability of Biological Macromolecules*", ed. S.N. Timasheff and G.D. Fasman, Marcel Dekker, New York, (1969).
- Hoernschemeyer, D.L., Lawrence, R.W., Saltonstall, C.W. and Schaeffler, O.S. Jr.; "Stabilization of cellulosic desalination membranes by crosslinking", in *Reverse Osmosis Membrane Research*, ed. by H.K. Lonsdale and H.E. Podall, Plenum Press, New York-London, 163-176, (1972).
- Jackson, J.M. and Landolt, D.; "About the mechanism of formation of iron hydroxide fouling layers on RO membrane", *Desalination*, 12, 361-378, (1973).

Johnson, A.R.; "Concentration polarization in RO under natural convection", Ph. D. thesis, Stanford University, (1970).

Johnson, J.S., Dresner, L. and Kraus, K.A.; "Hyperfiltration, in Principles of Desalination", K.S. Spiegler, Ed. 346-439, Academic Press, New York, (1966).

Josefson, A.J. and Munson, L.R.; "Ultrafiltration of Electro-coating Systems, Nonpolluting coatings and coating Processes", Proc. A.C.S. Symp., 69, (1973).

Keilin, B., OSW Res. Develop. Prog. Rept. 117, (1964).

Keller, K.H., Canales, E.R. and Su Il Yum; "Tracer and mutual diffusion coefficients of proteins", J. Phys. Chem., 75, 379-87, (1971).

Kesting, R.E. and Eberlin, J.; J. Appl. Polym. Sci., 10, 961 (1966).

Kimura, S. and Sourirajan, S.; AIChE, 13, 497, (1967).

Kimura-Yeh, F., Hopfenberg, H.B. and Stannett, V.; "The preparation and properties of styrene grafted cellulose acetate membranes for desalination", in Reverse Osmosis Membrane Research, ed. H.K. Lonsdale and H.E. Podall, 177-204, Plenum Press New York-London, (1972).

King, W.M., Hoernschmeyer, D.L. and Saltonstall, C.W. Jr.; "Cellulose acetone blend membranes", in Reverse Osmosis Membrane Research, ed. Lonsdale, H.K. and Podall, H.E., 131-162, Plenum Press New York-London, (1972).

Kottwitz, F.A. and Boylan, D.R.; "Prediction of resistance in constant pressure cake filtration", AIChE J., 4, 175-80, (1958).

Kozinski, A.A.; "Ultrafiltration of protein solutions", Ph. D. thesis Univ. of Wisconsin, (1971).

Kozinski, A.A. and Lightfoot, E.N.; "Ultrafiltration of proteins in stagnation flow", AIChE J., 17, 81-85, (1971).

Kozinski, A.A. and Lightfoot, E.N.; "Protein ultrafiltration: a general example of boundary layer filtration", AIChE Journal, 18, 1030-40, (1972).

Kuhn, W.; "Grenze der Durchlässigkeit von Filtrier- und Löslichkeitsmembranen", Zeitschrift f. Elektrochemie, 55, 207-217, (1951).

Kreula, M., Kiviniemi, L., Vuorinen, E. and Heikonen, M.; "The design of an ultrafiltration process for whey and skim milk", Milchwissenschaft, 29, (3), 129-137, (1974).

Kuiper, D., Bom, C.A., van Hezel, J.L. and Verdouw, J.; "The use of RO for the treatment of river Rhine water", Proceedings 4th int. symposium fresh water from the sea, Heidelberg, August 1973, 4, 207-215, (1973).

Lai, J.Y. and Nickelson, R.L.; paper at 21st Canadian Chemical Engineering Conference, Montreal, Quebec, 12-15, (Oct. 1971).

- Leiserson, L.; "Pretreatment, scale control and prevention of fouling in membrane separation processes", Proceedings of workshop symposium Membranes in Separation Process, at Case Western Reserve University, 143-146, (May 1973).
- Lim, T.H., Dunkley, W.L. and Merson, R.L.; "Role of protein in RO of cottage cheese whey", *J. Dairy Sci.*, 54, 306-311, (1971).
- Liu, M.K.; "Iterative analysis of a continuous system for desalination by reverse osmosis", *Desalination*, 9, 181-191, (1971).
- Liu, M.K.; "Perturbation analysis of a continuous system for desalination by RO", *Appl. Sci. Res.* 26, 349-60, (1972).
- Liu, M.K. and Williams, F.A.; "Concentration polarization in an unstirred batch cell: measurements and comparison with theory", *Int. J. Heat Mass Transfer*, 13, 1441-57, (1970).
- Lolachi, H.; "Application of fluidized bed for controlling the concentration polarization boundary layer in RO desalination system", *OSW Res. Progress Rept.* 843, (March 1973).
- Lonsdale, H.K., Merten, U. and Tagami, T.; *J. Appl. Polymer Sci.* 11, 1807, (1967).
- Lonsdale, H.K. and Podall, H.E.; "Reverse osmosis membrane research", Plenum Press, New York-London, (1972).
- Low, B.W. and Richards, F.M.; "Density, composition and unit cell dimensions of protein crystals", *J. Am. Chem. Soc.*, 76, 2511-18, (1954).
- Lowe, E. and Durkee, E.L.; "Dynamic turbulence promotion in RO-processing of liquid foods", *J. Food Sci.*, 36, 31-32, (1971).
- Madsen, R.F.; "Membrane concentration in Advances in Preconcentration and Dehydration of Foods", ed. A. Spicer, Applied Science Publishers, London, (1974).
- Madsen, R.F.; 1974 a) personal communication.
- Madsen, R.F.; in discussion at Membrane Filtration Workshop of the Danish Society of Dairy Technology, Vejle, (1974 b).
- Mastromonico, C.; "Reverse Osmosis in Laminar Flow in Annuli", M.S. Thesis, Clarkson College of Technology, Potsdam, N.Y. (1968).
- McCutchan, J.W. and Johnson, J.S.; *J.A.W.W.A.*, 62, 346, (1970).
- McKenzie, H.A., Raiston, G.B.; "Nature of products formed by the action of urea on bovine β -lactoglobuline", *Austral J. Biol. Sci.* 26, 859-870, (1973).
- Merson, R.L., Ginnette, L.F. and Morgan, A.I.; "Reverse osmosis for food processing", *Dechema Monographien*, 63, 179-201, (1968).
- Merson, R.L. and Ginnette, L.F.; "Improved processing of foods by RO", in *Applied Polymer Symposia* no. 13, *Membranes from Cellulose and Cellulose Derivatives*, ed. Turbak A.F., 309-322, Wiley, (1970).
- Merten, U.; *Ind. Eng. Chem. Fundamentals*, 2, 229, (1963).

- Merten, U., Lonsdale, H.K. and Riley, R.L.; *Ind. Eng. Chem. Fundam.*, 3, 210-213, (1964).
- Michaels, A.S., Nelsen, L. and Porter, M.C.; "Ultrafiltration", in *Membrane Processes in Industry and Biomedicine*, Bier, M., editor, Plenum Press, New York, (1971).
- Michaels, A.; in discussion, *Proceedings of workshop symposium Membranes in Separation Processes at Case Western University*, 142, (May, 1973).
- Minturn, R.E.; "Calcium sulfate scaling in RO of brackish waters by hollow fiber and spiral wound modules", *OSW Res. Develop. Progress Rept.* 897, (Oct. 1973).
- Monge, L.E., McCoy, B.J., Merson, R.L.; "Improved RO permeation by heating", *J. Food Sci.*, 38, 633-36, (1973).
- Muhlenkamp, S.P. and Srinivasan, S.; "Combination forced and free convection in RO for horizontal flows", *Proceedings of the 4th int. symposium on fresh water from the sea, Heidelberg, August 1973*, 4, 251-258, (1973).
- Mylius, U.V. and Saier, H.D.; "Versuche zur Proteinrückgewinnung aus Molke mit verbesserten Ultrafiltrationsmembranen", *Deutsche Milchwirtschaft, Hildesheim*, 11, 307, (1974).
- Nakano, Y., Tien, C. and Gill, W.N.; "Nonlinear convective diffusion: A hyperfiltration application", *AIChE Journal*, 13, 1092-98, (1967).
- Nunge, R.J. and Adams, L.R.; "Reverse osmosis in laminar flow through curved tubes", *Desalination*, 13, 17-36, (1973).
- Ogston, A.G.; "When is pressure osmotic", *Federation Proceedings*, 25, 1112-14, (1966).
- Oncley, J.L., Scatchard, G., Brown, A.; "Physical-chemical characteristics of certain of the proteins of normal human plasma", *J. phys. and colloid chemistry*, 51, 184-198, (1947).
- Peri, C. and Dunkley, W.L.; "RO of cottage cheese whey", Part 1 and Part 2, *J. Food Sci.*, 36, 25-30, (1971) and *J. Food Sci.*, 36, 395-396, (1971).
- Peri, C. and Pompei, C.; "Concentration and purification of milk and whey proteins by ultrafiltration", *Int. Symposium on heat and mass transfer problems in food engineering, Wageningen*, (Oct. 1972).
- Peri, C., Battisti, P. and Setti, D.; "Solute transport and permeability characteristics of RO membranes", *Lebensm. Wiss, Technol.*, 6, 127-132, (1973).
- Perutz, M.F.; "Proteins and Nucleic Acids", Elsevier, Amsterdam/London/New York, (1962).
- Pihl, P., Alfa-Laval Lund, private communication, (1974).
- Pitera, E.W. and Middleman, S.; "Convection promotion in tubular desalination membranes", *Ind. Eng. Chem. Process Des. Develop.*, 12, 52-56, (1973).

Porter, M.C.; "Concentration Polarization with Membrane Ultra-filtration", Ind. Eng. Chem. Prod. Res. Develop., 11, 3, 234-248, (1972).

Pusch, W. and Staude, E.; "Reflection coefficient and solute rejection of asymmetric cellulose acetate membrane using phenol solutions", paper at 4th int. symposium Fresh water from the sea, Heidelberg, August 1973.

Ramanadhan, K. and Gill, W.N.; "Cominbed forced and free convective diffusion in vertical semipermeable parallel plate ducts", presented at the AIChE Meeting, Tampa, (May, 1968).

Raridon, R.J., Dresner, L. and Kraus, K.A.; Desalination, 1, 210, (1966).

Reid, C.E., "Reverse Osmosis", Nat. Acad. Sci. Nat. Res. Council, Publication 568, 238, (1958).

Reid, C.E.; Principles of Reverse Osmosis, in "Industrial Processing with Membranes", ed. Lacey, R.E., Loeb, S., Wiley Interscience, New York, (1972).

Richardson, J.L., Segovia, G., Baerg, W. and Anderson, M.; "RO tubular module optimization", OSW Res. Dev. Progr. Rept. 455, (1969).

Riley, R.L., Lonsdale, H.K., Lyans, C.R. and Merten, U.; J. Appl. Poly. Sci., 11, 2143, (1967).

del Rosario, N.O. and Siao Fang Sun; "On the aggregation of bovine serum albumin in 0.1 M salt solutions", Can. J. Chem., 51, 3781-88, (1973).

Rosenblatt, N.W.; "Desalination with an asymmetric amidehydrazide membrane", Proceedings of the 4th int. symposium on fresh water from the sea, Heidelberg, August 1973, 4, 349-361, (1973).

Rossi Fanelli, A., Antonini, E. and Caputo, A.; "Hemoglobin and Myoglobin", in Advances in Protein Chemistry, eds C.B. Anfinsen et al, Vol. 19, 74-223, Academic Press, New York and London, (1964).

Ruth, B.F.; "Correlation filtration theory with industrial practice", Industr. Engng. Chem. (Industr.), 38, 564-71, (1946).

Scatchard, G., Batchelder, A.C., Brown, A., Zosa, M.; "Osmotic equilibria in concentrated solutions of serum albumin", J. Am. Chem. Soc., 68, 2610-2612, (1946).

Scattergood, E.M. and Lightfoot, E.N.; "Diffusional interaction in an ion exchange membrane", Farad. Soc. Trans., 54, 1135-1146, (1968).

Schlögl, R.; "Stofftransport durch Membranen", Steinkopff Verlag, Darmstadt, (1964).

Schmidt, A.; Phys. Chem., 99, 337, (1856).

Shah, Y.T.; "Mass transport in RO in case of variable diffusivity", MSc thesis, Univ. of Pittsburgh, Pennsylvania (1969), even Int. J. Heat Mass Transfer, 14, 921-929, (1971).

- Shaw, R.A., Deluca, R. and Gill, W.N.; "Reverse osmosis: Increased productivity by reduction of concentration polarization in laminar flow reverse osmosis using intermediate non-rejection membrane sections", *Desalination*, 11, 189-205, (1972).
- Sheppard, J.D. and Thomas, D.G.; 1970 a, *Appl. Polym. Symp. Ser.*, 13, 121-128, (1970).
- Sheppard, G.D. and Thomas, D.G.; "Increased polarization caused by films covering hyperfiltration membranes", *AIChE Journal*, 17, 4, 910, (1971).
- Sheppard, J.D., Thomas, D.G. and Channabasappa, K.C.; "Membrane fouling part IV, Parallel operation of 4 tubular hyperfiltration modules at different velocities with feeds of high fouling potential", *Desalination*, 11, 385-389, (1972).
- Sherwood, T.K., Brian, P.L.T. and Fischer, R.E.; M.I.T. Desalination Res. Lab., Report 295-1, (1963).
- Sherwood, T.K., Brian, P.L.T., Fischer, R.E. and Dresner, L.; "Salt concentration at phase boundaries in desalination by RO", *Ind. Eng. Chem. Fundamentals*, 4, 113-118, (1965).
- Sherwood, T.K., Brian, P.L.T. and Fischer, R.E.; "Desalination by RO", *Ind. Eng. Chem. Fundamentals*, 6, 2-12, (1967).
- Sivik, B.; "Processing of potato juice", report (in Swedish) to Dept. Food Eng., Lund University, (1974).
- Sourirajan, S.; "Reverse Osmosis", Logas Press Ltd., London, (1970).
- Sourirajan, S. and Matsuura, T.; "Physicochemical criteria for RO separation of inorganic and organic solutes in aqueous solutions using porous cellulose acetate membranes", *Proceedings of workshop symposium, "Membranes in separation Processes"*, at case Western Reserve University, (May, 1973).
- Srinivasan, S. and Tien, C.; "RO desalination in tubular membrane duct", *Desalination*, 3, 5-16, (1967).
- Srinivasan, S. and Tien, C.; "RO in multicomponent systems", *Desalination*, 5, 139-156, (1968).
- Srinivasan, S. and Tien, C.; "Reverse osmosis in a curved tubular membrane duct", *Desalination*, 9, 127-139, (1971), (for comput. errors in this work see even *Desalination* 12, 277, (1973).
- Srinivasan, S. and Tien, C.; "Effect of imperfect salt rejection on concentration polarization in reverse osmosis systems", *Desalination*, 13, 287-301, (1973).
- Srinivasan, S., Tien, C. and Gill, W.N.; *Chem Eng. Sci.*, 22, 417, (1967).
- Strathmann, H.; "Control of concentration polarization in RO desalination of Water", *OSW Res. Dev. Progr. Rept.*, 336, (April 1968).
- Strathmann, H.; "Untersuchungen zur Konzentrationsüberhöhung bei der Membranfiltration", *Chemie Ing. Techn.*, 44, 1160, (1972).

Strathmann, H.; "Untersuchungen zur Konzentrationsüberhöhung bei der Membranfiltration. Teil II: Konzentrationsüberhöhung bei der Filtration von Makromolekularen Lösungen", Chemie Ingenieur Technik, 12, 825-832, (1973).

Tanford, Ch.; "Physical Chemistry of Macromolecules", John Wiley Inc. New York, 5th printing 1967, 383, (1961).

Thomas, D.G., Hayes, P.H., Mixon, W.R., Sheppard, J.D., Griffith, W.L. and Keller, R.M.; "Turbulence promoters for hyperfiltration with dynamic membranes", Environm. Sci. and Techn., 4, 12, 1129-1135, (1970).

Thomas, D.G., Griffith, W.L. and Keller, R.M., "The role of turbulence promoters in hyperfiltration plant optimization", Desalination, 9, 33-50, (1971).

Thomas, D.G.; "Estimation of concentration polarization for ion-exclusion hyperfiltration membranes with turbulent flow", Ind. Eng. Chem. Fundam., 11, 302, (1972).

Thomas, D.G. and Watson, J.S.; Ind. Eng. Chem. Process Des. Develop., 7, 397, (1968).

Thomas, D.G. and Mixon, W.R.; effect of axial velocity and initial flux on flux decline of cellulose acetate membranes in hyperfiltration of primary sewage effluents, Ind. Eng. Chem. Process Des. Develop., 11, 339, (1972).

Thomas, D.G.; Ind. Eng. Chem. Fundamentals, "Forces convection mass transfer in hyperfiltration at high fluxes", 12, 396-405, (1973).

Tien, C. and Gill, W.N.; AIChE Journal, 12, 722, (1966).

Tiller, F.M.; "The role of porosity in filtration", Chem. Eng. Progress, 49, 467-79, (1953).

Traube, M.; Archiv. Anat. Physical, 86, (1867).

Tsao, C.K.; Desalination, 8, 234-258, (1970).

Tsao, C.K.; -quoted by Goldsmith and Lolachi, (1971).

Van Oss, C.J. and Bronson, P.M.; "Characteristics of a protein concentrating anisotropic cellulose acetate membrane", Separation Sci., 5, 63-75, (1970).

Vos, K.D., Burris, F. and Riley, R.L.; J. Appl. Polymer Sci., 10, 825, (1966).

Wang, J.H., Anfinson, Ch. B. and Polestra, F.M.; "The self diffusion coefficients of water and ovalbumin in aqueous ovalbumin solutions at 10°C", J. Am. Chem. Soc., 76, 4763-4765, (1954).

Welinder; Tekn. lic. thesis, Dept. Chem. Ind., Technical University of Denmark, Lyngby, (1974).

White, A, Handler, P., Smith, E.L.; Principles of Biochemistry, 4th ed. 124, McGraw Hill/Kogakusha, (1968).

- Wiley, A.J., Ammerlaan, A.C.F. and Dubey, G.A.; Application of RO to processing spent liquors from the pulp and paper industry, Tappi, 50, 455-60, (1967).
- Wiley, A.J., Dubey, G.A. and Bansal I.K.; "RO concentration of dilute pulp and paper effluents", Report to EPA on EPA WQ Contract no. 12040 EEL, (Febr. 1972).
- Wiley, A.J., Scharph, K., Bansal, I. and Arps, D.; Reverse osmosis concentration of spent liquor solids in press liquors from high-density pulps, Tappi, 55, 12, 1671-1675, (1972).
- Williams, F.A.; "Some properties of the solution to a non-linear diffusion problem relevant to desalination by reverse osmosis", Siam J. Appl. Math, 17, 59-73, (1969).
- Williams, F.A.; "Boundary Layer Flow problems in Desalination Reverse Osmosis", Univ. of California, San Diego, AMES-QR-220-3 (Sept. 1967).
- Williams, F.A. and Hendricks, T.J.; "Boundary layer flow problems in desalination by RO", OSW Quarterly Rept. (Sept. 1967).
- Williams, F.A., Hendricks, T.J. and Liu, M.K.; "Boundary layer flow problems in desalination by RO", OSW Res. Dev. Progr. Rept. 622, (Dec. 1970).
- Wilson, A.D.; "Partial concentration of whey by reverse osmosis", N.Z. Journal Dairy Sci. Techn., 7, 3, (1972).
- Winograd, Y. and Solan, A.; "Concentration build-up in RO in turbulent flow", Desalination, 7, 97, (1969).
- Winograd, Y., Toren, M. and Solan, A.; "Reverse osmosis in shell and tubes", Desalination 14, 173-187, (1974).
- Yi Yan, A.; "Reflection studies in membrane deterioration", Proceedings 4th int. symposium on fresh water from the sea, Heidelberg, August 1973, 4, 443-448, (1973).
- Young, E.G.; Occurrence, classification, preparation and analysis of proteins, in Comprehensive Biochemistry Ed. M. Florkin and E.H. Stotz, Elsevier, New York, (1963).
- Zeh, D.W. and Gill, W.N.; AIChE Journal, 13, 1014, (1967).
- Zeh, D.W. and Gill, W.N.; AIChE Journal, 14, 715, (1968).
- Zumbro, F.R.; Du Pont-Dept. Public affairs, letter of Nov. 20, (1974).

Appendix A: The drop interval meter

A block scheme of the apparatus is given in Fig. A1. An IR light emitting diode - phototransistor combination detects the passage of a drop. The signal is after amplification fed to a Schmitt trigger and then to two monostable vibrators. The output pulse of the first vibrator transfers the charge from the integrator circuit to the storage condenser. Subsequently, after the transfer FET switch has closed, the pulse from the other vibrator resets the integrator to zero.

The output of the meter is approximately proportional to the time interval between drops. Besides inaccuracy of the time base, the loss of time before the integrator is reset causes some nonlinearity. However, it was found that a more significant cause of nonlinearity of the device when used as $\frac{1}{F_{\text{low}}}$ meter is the size of drops. Apparently, at drop frequencies higher than 1 per second drop size increases significantly. In addition, the equipment suffered long-term drift. On the other hand, the meter was not affected by presence of salt, urea or protein in the measured solution. Air in the permeate lines interfered with measurement, causing unstable readings. For conversion of recorder reading to $\frac{1}{F_{\text{low}}}$ value, a calibration curve was used. The calibration curve was checked at least once daily. Maximum scatter of data ever was about 6 %. The 4 sets of calibration data over a randomly chosen 10 days period, including one 8 M urea run are shown in Fig. A2.

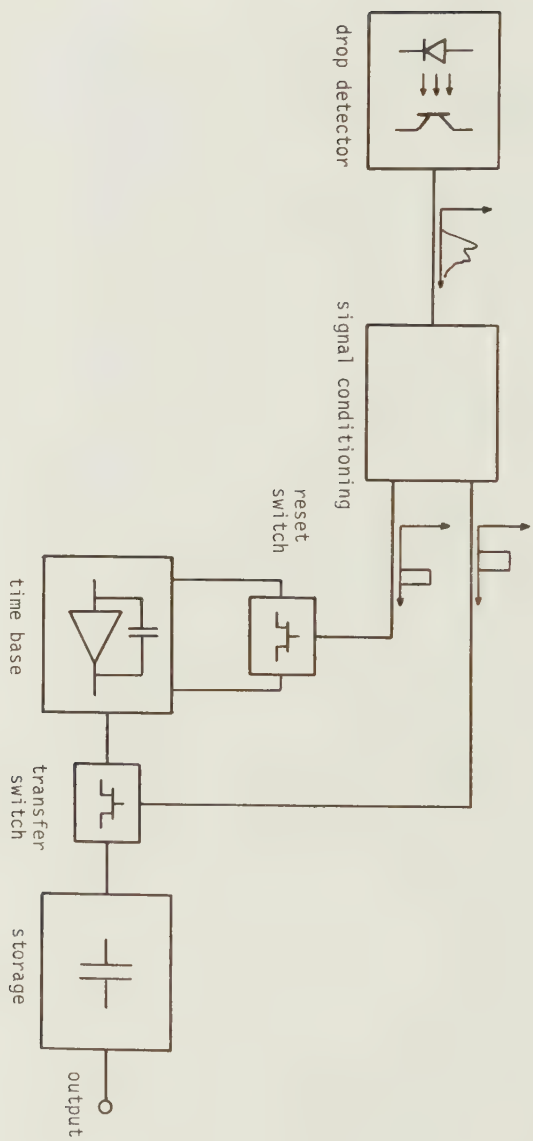


Fig. A-1: Drop interval meter.

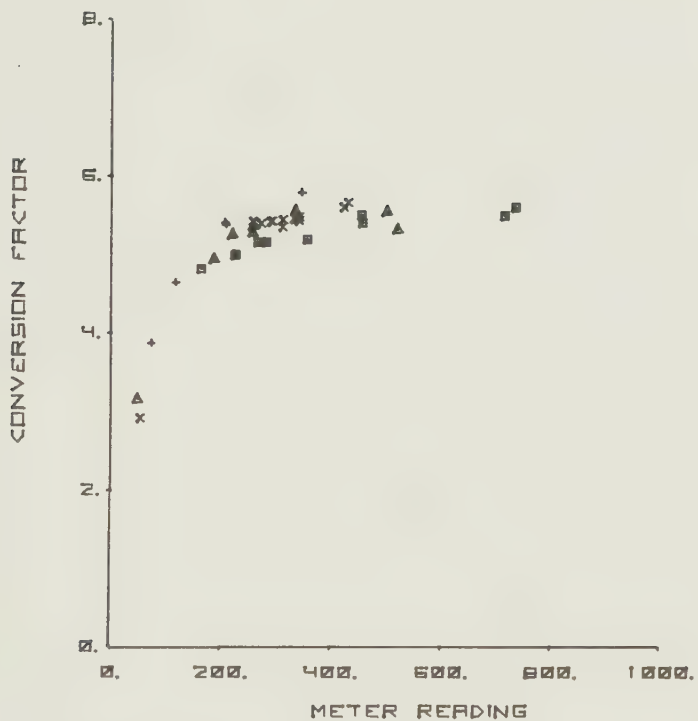


Fig. A-2: Calibration of the drop interval meter.

Appendix B: Membrane casting apparatus.

An apparatus to cast semicontinuously ultrafiltration membrane was designed and built.

The membrane is cast on the surface of an ordinary aluminium foil sold in rolls of 30 m length as kitchen utensil. As sketched, Fig. B-1, the foil is drawn between two polished steel cylinders down into the coagulation bath and wound up on a take-up roll, which is driven by V-belt from a variable speed motor. The casting solution is poured into the trough formed by the cylinders and is drawn out as a film through the adjustable slit between them. It coagulates in cold water bath and peels off the foil as the foil is taken up by the driving roll. After the casting run, the membrane is left in the bath for leaching in at least an hour.

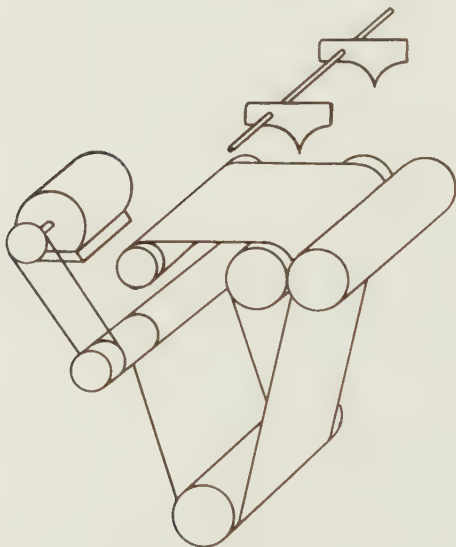


Fig. B-1: Membrane casting apparatus.

Appendix C: Solubility of lysozyme.

To determine roughly the solubility, 0.7 g lysozyme was suspended in 1 ml water and kept in cold overnight. Next day it was equilibrated to room temperature, its pH checked, it was centrifuged, a sample of the supernatant was taken and absorbance at 280 nm read. The rest was pH adjusted with 10 M NaOH and kept in cold to the following day. If necessary, more water was added. The absorbances were converted to concentrations using $A_{1\%} = 26.2$

Table C-1

pH	5.45	6.05	8.65	9.35	9.50	10.42	11.00
ionic strength	0.05	0.05	0.075	0.053	0.066	0.079	0.092
solubility (mg/ml)	263	370	240	33	6.9	1	1.5

Appendix D

Table D - 1: bovine plasma albumin.

Concentration calculated from absorbance $A_{280} \% = 6.5$

Membrane resistance in practical units. Multiply by $1.5 \cdot 10^5$ to obtain bar/m s^{-1}

Specific gel resistance in practical units. Multiply by $3.75 \cdot 10^{13}$ to obtain s^{-1} .

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.15M NaCl	6.3	45	1	DDS 600	0.93	0.15	2.56	2.56
0.15M NaCl	6.3	45	1	DDS 600	0.90	0.14 0.12	2.56 2.20	2.56 2.56
0.15M NaCl	7	18	0.2	CA 50	0.35	0.055	1.04	1.04
0.2M phosphate	7	10	0.2	DDS 600	1.63	0.205 0.28 0.13 0.11	2.45 2.7 1.35 0.45	2.45 4.3 2.45 1.1
0.2M phosphate	7	10	0.2	CA 50	0.36	0.12	1.90	2.48
0.15M NaCl	2	25	0.50	CA 50	0.32	0.20 0.204	2.81 3	3 3

0.15M NaCl	2	50	1	CA 50	0.32	0.20 0.204	2.9 3	3 3
0.15M NaCl	7	50	1	CA 50	0.33	0.14 0.154	2.95 3.11	3.11 3.11
0.15M NaCl	7	25	0.5	CA 50	0.33	0.156 0.178	2.89 3.11	3.11 3.11
0.15M NaCl	7	50	1	CA 50	0.35	0.117 0.11	2.3 3.1	3.1 3.1
0.15M NaCl	7	25	0.5	CA 50	0.37	0.116 0.135	2.74 3.1	3.1 3.1
0.15M NaCl	6.7	30	0.6	CA 50	0.31	0.126 0.154	2.72 2.94	2.94 2.94
0.15M NaCl	6.7	30	0.6	CA 50	0.32	0.143 0.18	2.75 2.94	2.94 2.94
0.15M NaCl	6.8	30	0.6	DDS 975	3.52	0.05	0.89	2.97
0.15M NaCl	6.9	30	0.6	DDS 975	2.9	0.093 0.112	1.46 2.95	2.95 2.95
0.15M NaCl	6.8	30	0.6	DDS 975	4.02	0.09	1.19	2.95

Table D 1 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.1M Na ci- trate-HCl	1.7	25	0.5	CA 50	0.3	0.059	0.83	1
						0.082	1.74	2
						0.11	2.70	3
						0.124	3.65	4
						0.087	1.76	2
0.15M NaCl	7	25	1	DDS 800	1.56	0.10	2.4	3.9
						0.82	1.7	3
						0.054	0.84	1.8
						0.035	0.36	1
0.15M NaCl	7	25	1	DDS 975	5.36	0.061	0.88	4
0.15M NaCl +0.01 g/l bromphenol blue	4.65	25	0.5	CA 50	0.30	0.07	0.85	1
						0.108	1.8	2
						0.140	2.76	3
						0.168	3.73	4
						0.16	3.72	4
						0.06	0.83	1
						0.10	1.79	2
						0.136	2.75	3
0.1M Na-Ci- trate-HCl	1.7	25	1	CA 50	0.27	0.167	3.76	4
						0.15	2.8	3
0.15M NaCl	6.1	25	0.5	CA 50	0.30	0.174	3.76	4.04
						0.100	1.77	1.98

0.005M NaCl	7	30	0.6		CA 50	0.3	0.126 0.164 0.087 0.115 0.116 0.146 0.081 0.110	2.8 3.8 1.7 2.76 2.75 3.75 1.7 2.65	3 4.05 1.9 3 3 4.05 1.95 2.9
0.005M NaCl	7	30	0.6		CA 50	0.31	0.120 0.148 0.076	2.85 3.83 1.63	3.1 4.1 1.85
0.15M NaCl	7.1	25	1		CA 50	0.29	0.16 0.129 0.19	3.71 2.75 4	4 3 4
0.15M NaCl	7.2	100	1		CA 50	0.27	0.19	4	4
0.15M NaCl	7	100	2		CA 50	0.29	0.192	4	4
0.15M NaCl	6.9	100	2		CA 50	0.30	0.14	2	2
0.15M NaCl	7.1	100	1		DDS 870	6	0.13	4	4
0.15M NaCl	7	100	1		4 x CA 50	1.16	0.191	4	4
0.15M NaCl	3.05	10	1		CA 30	1	0.208	4	4
0.15M NaCl	7.05	10	1		4 x CA 50	1.23	0.196	4	4
0.15 NaCl	7	50	5		CA 50	0.29	0.227	4	4
							0.192	4	4
							0.180	4	4
							0.194	4	4
8 M urea		20	1		CA 35	0.99	0.254	4	4
9.15 NaCl		20	1		CA 35	0.99	0.206	4	4
8 M urea		20	1				0.280	4	4

Table D 1 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.15M NaCl	7	30	1	CA 50	0.27	0.065 0.104 0.195	1 2 4	1 2 4
0.15M NaCl	6.9	52	4	CA 50	0.31	0.167 0.117 0.062	4 2 1	4 2 1
Dest. water	2.0	25	1	CA 50	0.26	0.108 0.99	3.65 2.74	4 3
0.01M NaCl dest. water	2.0	15	0.6	CA 50	0.25	0.127 0.091	3.54 3.58	4 4
0.05M NaCl	2					0.127	3.52	4
0.1M NaCl	2					0.153	3.59	4
0.2M NaCl	2					0.160	3.63	4
0.3M NaCl	2					0.223	3.72	4
0.5M NaCl	1.9					0.353	3.82	4
1 M NaCl	2					0.353	3.82	4
3 M NaCl	2					0.733	3.98	4
						2.01	4	4
						1.79	2.95	2.95
						1.59	2	2
						1.23	1	1
						0.93	0.5	0.5

0.15M NaCl	40	0.5	CA 35	0.77	0.206	4	4
0.15M NaCl	40	0.5	CA 50	0.32	0.123	1.7	1.7
0.15M NaCl	40	0.5	CA 50 +	1.11	0.263	6.09	6.09
0.15M NaCl	6.7 30	0.6	CA 35	0.28	0.024	0.37	0.52
0.15M NaCl	28.8	0.6	CA 50	0.31	0.123	2.73	2.97
0.15M NaCl +	30	0.6	CA 50	0.3	0.097	2.52	2.78
0.001 % Tween 80							
0.15M NaCl	6 25	0.5	CA 50	0.33	0.188	4	4
					0.148	3	3
					0.182	3.72	4
0.15M NaCl	6 25	0.5	CA 35	0.96	0.182	4	4
					0.156	3	3
					0.106	2	2
					0.048	1	1
					0.181	3.3	4
					0.140	2.38	3
					0.11	1.27	2
					0.065	0.63	1
0.15M NaCl	5.8 25	0.5	3 x CA 35	2.71	0.113	2.03	4
					0.084	1.33	3.05
					0.061	0.73	2.02
					0.048	0.33	1.09
					0.117	2.07	4
0.15M NaCl	6.2 25	0.50	CA 50	0.31	0.14	3.81	4.15
					0.11	2.62	2.92
					0.077	1.56	1.8

Table D-2: Hemoglobin.

Membrane resistance in practical units. Multiply by $1.5 \cdot 10^5$ to obtain bar/m s^{-1} .
Specific gel resistance in practical units. Multiply by $3.75 \cdot 10^{13}$ to obtain s^{-1} .

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.15M NaCl	5.2	15.7	0.33	CA 35	0.60	0.075	0.68	1.03
						0.310	4.76	5.35
						0.250	3.55	4.09
						0.197	2.54	3.03
						0.142	1.62	2.06
						0.078	0.67	0.99
0.15M NaCl	2.4	16.2	0.33	CA 35	0.62	0.331	4.80	5.35
						0.265	4.64	5.29
						0.251	3.50	4.04
						0.221	2.63	3.08
						0.190	1.66	2
						0.147	0.857	1.08

Table D 2 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.1M Citrate (solution aged 3 days)	4.1	32	0.64	CA 50	0.33	0.681 0.711 0.725 0.731	1.3	1.3
							2.1	2.1
							3.2	3.2
							4.4	4.4
0.1M Citrate	4	32	0.64	CA 50	0.32	1.17 1.28 1.34 1.45	1.25	1.25
							1.9	1.9
							2.9	2.9
							4.4	4.4
0.1M Phos- phate	6.8	32	0.64	CA 50	0.32	0.273 0.183 0.134 0.223	4.1	4.25
							2.2	2.32
							1.38	1.48
							2.92	3.05
0.15M NaCl	7.9	94	1.88	CA 50	0.30	0.366	4	4
0.15M NaCl	7.55	15.7	0.33	CA 50	0.29	0.325 0.272 0.194 0.131 0.356	3.80	4.02
							2.84	3.03
							1.74	1.90
							0.96	1.09
							3.82	4.02

Table D 2 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.33M Na ₂ SO ₄	7.4	12.5	0.42	CA 50	0.32	0.071	0.5	0.5
0.66M Na ₂ SO ₄	6.88	7.5	0.26		0.42	0.135	0.6	0.6
1 M Na ₂ SO ₄	7	8.1	0.37		0.37	0.122	0.65	0.65
1.33 Na ₂ SO ₄	6.9	3.6	0.19		0.33	0.19	0.5	0.5
0.33M Na ₂ SO ₄	6.78	46.8	3.1	CA 50	0.31	0.053	0.5	0.5
0.66M Na ₂ SO ₄	7.5	53	3.40		0.38	0.072	0.6	0.6
1 M Na ₂ SO ₄	7.61	39.3	3.0		0.35	0.091	0.65	0.65
1.33M Na ₂ SO ₄	7.54	23.2	1.76		0.32	0.057	0.5	0.5
1 M NaCl	7.34	33	0.69	CA 50	0.30	0.068	0.53	0.6
0.33M Na ₂ SO ₄	7.37	29.4	0.66	CA 50	0.30	0.073	0.53	0.6
0.15M NaCl	5.4	15.7	0.33	CA 50	0.30	0.123 0.072 0.268	1.39 0.60 3.73	1.6 0.76 4
0.15M NaCl	4.35	15.7	0.33	CA 50	0.30	0.514 0.462 0.357 0.286	3.86 2.98 1.75 1.03	4 3.1 1.84 1.1

0.15M NaCl	3.40	16.2	0.33	CA 50	0.29	0.407 0.365 0.323 0.250 0.428	3.83 2.75 1.90 1.12 3.83	4 2 1.2 4
0.15M NaCl	2.35	16.2	0.33	CA 50	0.29	0.271 0.250 0.215 0.166 0.314	3.74 2.82 1.80 0.99 3.78	4 3.02 1.95 1.1 4
0.15M NaCl	6.35	15.7	0.33	CA 35	0.59	0.325 0.085 0.129	4.74 0.77 1.56	5.29 1.11 2.01
0.1M Phos- phate	7.45	15.7	0.33	CA 50	0.62	0.339 0.254 0.191 0.109 0.418	3.62 2.44 1.65 0.74 4.84	4.02 2.81 1.99 1 5.26
0.1M Citrate	4	10	0.2	CA 50	0.48	1.25 1.2 1.03 1.7	3.5 3.3 1.8 0.9	3.5 3.5 1.9 0.93
0.1M Citrate	4	10	0.2	CA 50	0.32	1.15 1.15 1.0 1.0	3.5 3.4 1.83 0.9	3.5 3.5 1.9 0.93

Table D 2 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.15M NaCl		50	1	CA 50	0.33	0.264 0.19	4.2 2.9	4.3 3
		50	1	CA 50	0.37	0.30 0.26 0.20 0.196 0.156 0.116 0.068 0.056	3.9 3.2 2.28 2.03 1.55 0.95 0.6 0.55	4 3.3 2.35 2.1 1.6 1 0.65 0.6
0.025M Citrate		50	1	CA 50	0.33	0.40 0.34 0.36 0.29 0.23 0.124 0.094	4.92 4.82 4.85 3.9 2.9 1.34 0.71	4.92 4.92 4.95 4 3 1.4 0.75
		25	0.8	CA 50	0.33	0.175 0.215	0.62 0.68	0.68 0.68
0.025M Citrate		50	0.8	CA 50	0.32	0.108 0.625 0.55 0.238 0.13	0.68 4.74 3.84 1.36 0.64	0.68 4.8 3.9 1.4 0.68

0.15M NaCl 0.025 Citrate 0.1M Citrate			0.8 0.8 0.8		CA 50	0.35	0.083 0.125 0.74	0.72 0.78 0.70	
0.025M Citrate	4		0.8		DDS 600	1	0.225	0.82	0.82
0.025M Citrate	4.1		0.8		CA 50	1	0.375	1.12	1.12
0.15M NaCl	7.25	38	0.62		CA 50	0.32	0.089	0.5	0.5
0.1M Citrate	3.95	9.2	0.62		CA 50	0.32	0.93	0.5	0.5
0.1M Citrate	3.95	4	0.62		CA 50	0.43	0.86	0.5	0.5
0.15M NaCl	7.5	7	0.08		CA 50	0.31	0.12	1.28	1.28
0.15M NaCl	7.5	11	0.31		CA 50	0.31	0.096	1.28	1.28
0.15M NaCl	7.5	11	0.28		CA 50	0.30	0.056	0.65	0.65
0.15M NaCl	7.5	9	0.07		CA 50	0.31	0.15	1.86	1.86
0.15M NaCl	7.5	5	0.12		CA 50	0.31	0.052	0.6	0.6
0.15M NaCl	7.5	28	1.19		CA 50	0.38	0.068	0.7	0.7
0.15M NaCl	7.5	28	0.35		CA 50	0.30	0.067	0.72	0.72

Table D-3: β -lactoglobulin.Concentration calculated from absorbance $A_{1\%}^{280} = 9.5$ Membrane resistance in practical units. Multiply by $1.5 \cdot 10^5$ to obtain $\text{bar} \cdot \text{m} \cdot \text{s}^{-1}$.Specific gel resistance in practical units. Multiply by $3.75 \cdot 10^{13}$ to obtain s^{-1} .

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)	Leakage of solute
0.01M Acetate	6.05	26	0.53	CA 35	0.83	0.120 0.092 0.064 0.035 0.195	3.15 2.25 1.34 0.53 4	4 3 2 1 4	2 %
0.01M Acetate	5.1	21	0.46	CA 35	0.78	0.346	3.6	4	< 5 %
0.005M NaCl	5	25.3	0.505	CA 35	1.05	0.613	4	4	
0.005M (some aggre- gate)	4.8	22	0.44	CA 35	0.97	0.513 0.425 0.288 0.188	3.7 2.8 1.8 0.9	4 3 2.03 1.10	> 5 %

0.02M NaCl	5.41	16.8	0.84	CA 35	0.95	0.311	4	4	5 %
0.15M NaCl	7.1	84	0.84	CA 35	0.89	0.243	4	4	0
0.017M NaCl	7.2	20.4	0.82	DDS AR 8	1.56	0.104	1.15	2	< 10 %
0.15M NaCl	7.2	8.4	0.34	DDS AR 8	1.44	0.179	1.96	4	< 20 %
0.15M NaCl	7.2	5.9	0.24	DDS AR 8		0.172	2.15	4	< 10 %
0.005M NaCl	5.5	43	0.86	CA 50	0.3	0.40	3.1	3.1	12 %
0.15M NaCl	7	23.8	0.48	CA 50	0.36	0.191 0.193	3 2.75	3 3	20 %
0.15M NaCl	7	47.5	0.95	CA 50	0.36	0.218 0.198	2.9 2.8	2.9 2.9	10 %
0.15M NaCl	7	16	0.33	CA 50	0.35	0.191 0.192	2.95 2.56	2.95 2.95	25 %
0.15M NaCl	7	56	1.12	CA 50	0.36	0.230 0.211	3 2.9	3 3	5 %
0.15M NaCl	7	93	1.86	CA 50	0.38	0.222 0.23	2.94 3	3 3	6 %
8 M urea	7.5	23.2	0.93	DDS AR 8	1.36	0.215	1.6	2	0 %
8 M urea	7.8	19.8	0.79	DDS AR 8	1.15	0.200 0.239	1.6 2.07	2 2.07	5 %

Tabel D-3 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)	Leakage of solute
0.005M NaCl (some aggregate - heat denaturated at 750C)	4.8	24.7	0.495	CA 35	1.00	0.303	3.5	4	> 5 %
						0.230	2.6	3.07	
						0.163	1.6	2.01	
						0.092	0.73	1.05	
						0.358	4	4	
0.15M NaCl	4.8	24.7	0.495	CA 35	0.93	0.194	3.35	3.99	0
						0.158	2.4	3.06	
						0.109	1.5	2.06	
						0.061	0.64	1.04	
						0.24	4	4	
0.15M NaCl	4.8	24.7	0.495	CA 35	0.97	0.216	3.38	4	7 %
						0.052	0.58	1.02	
						0.109	1.49	2.03	
0.15M NaCl	5.25	19.2	0.97	CA 35	0.92	0.218	4	4	7 %
0.15M NaCl	5.8	19.2	0.97	CA 35	0.94	0.22	4	4	7 %
0.002M NaCl	5.35	15.6	0.78	CA 35	0.98	0.357	4	4	0
0.002M NaCl	5.5	16.6	0.83	CA 35	0.98	0.288	4	4	0
0.002M NaCl	5.85	16.4	0.82	CA 35	1.06	0.300	4	4	0
0.02M NaCl	5.25	17.7	0.89	CA 35	0.95	0.386	4	4	5 %

Table D-3 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)	Leakage of solute
8 M urea	7.6	19.5	0.78	DDS AR 8	1.39	0.231 0.256	1.5 2	2 2	< 5 %
8 M urea	7.3	20	0.8	DDS AR 8	1.28	0.197 0.249	1.52 2	2 2	3 %
6 M urea	7.7	18.9	0.76	DDS AR 8	1.38	0.250	2	2	3 %

Table D-4: Lysozyme.

Membrane resistance in practical units. Multiply by $1.5 \cdot 10^5$ to obtain bar/m s^{-1} .
 Specific gel resistance in practical units. Multiply by $3.75 \cdot 10^{13}$ to obtain s^{-1} .

NaCl ionic strength	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.00035	6.7	46	0.95	CA 25	3.25	0.051	2.08	2.08
						0.045	0.83	2.08
						0.053	1.72	4
						0.048	1.17	2.9
0.15	6.7	46	0.95	CA 25	3.58	0.043	0.41	1.08
						0.085	2.03	2.03
						0.10	2.3	4.05
						0.082	1.56	3
0.00035 0.15	8.8 8.3 8.6 8.5	47	1 1.69 0.79 1.92	CA 25	3.42	0.058	0.87	1.99
						0.035	0.32	1.01
						0.072	4.12	4.12
						0.066	4.12	4.12
						0.171	4.12	4.12
						0.212	4.12	4.12

0.15	6.2	44.5	0.95	CA 25	3.74	0.166 0.14 0.091 0.077 0.055	4 2.5 1.62 1 0.43	4 4 3.08 2.12 1.07
0.05	5.5	50	1	CA 35	0.95	0.15	4	4
0.075	8.9	17.2	0.34	CA 35	0.94	0.22	4	4
0.075	9.3	19.4	0.39	CA 35	0.96	0.25	4	4
0.1	10.15	22.3	0.49	CA 35	0.93	0.74	4	4
0.15	10.5	50	1	DDS AR 8	1.28	0.79	4	4
0.00035	10.5	50	1	DDS AR 8	0.85	0.50	4	4
0.00012	7.1	50	1	DDS 930	4.49	0.083 0.064 0.046 0.052 0.058 0.062 0.088	4 1.67 0.34 0.76 1.17 1.63 4	4 4 1 2.05 3 4 4
0.00014	7	25	0.46	DDS 930	4.11	0.13 0.05 0.062 0.068 0.076 0.12	4 0.23 0.57 0.88 1.26 4	4 1.02 2.07 3.01 4 4

Table D-4 (Continued)

NaCl ionic strength	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
0.00035	9.55		0.92	CA 25	3.35	0.056	4.12	4.12
0.00035	9.4		1.53			0.061	4.12	4.12
0.0008	9.55		1.92			0.119	4.12	4.12
0.15	9.3		0.76			0.196	4.12	4.12
						0.182	4.12	4.12
						0.063 (+)	2.08	2.08
						0.231	4.12	4.12
0.012	6.5	43	0.80	CA 25	3.42	0.068	4.15	4.15
	6.45		2.05			0.064	4.15	4.15
0.15	6		0.70			0.096	4.15	4.15
	6.02		1.28			0.122	4.15	4.15
	5.98		3.21			0.138	4.15	4.15
0.00035	6.5	50	1	CA 25	3.34	0.063	1.94	4.03
						0.061	1.48	3.08
						0.057	0.95	2.05
						0.061	0.53	1.09
						0.067	2	4.03
0.11						0.065	4.03	4.03
0.08						0.087	2	4.03
0.06						0.058	0.88	1.89
0.04						0.045	0.32	0.79
						0.075	2.18	4.11
0.15	7.2	50	1	CA 35	1.05	0.21	4	4

Table D-5: Blue Dextran.

Membrane resistance in practical units. Multiply by $1.5 \cdot 10^5$ to obtain bar/m s^{-1} .
Specific gel resistance in practical units. Multiply by $3.75 \cdot 10^{13}$ to obtain s^{-1} .

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
Dest. water		50	1	CA 50	0.36	0.18	0.95	0.95
						0.38	4.3	4.3
						0.31	3.1	3.1
						0.24	1.85	1.85
						0.15	0.91	0.95
Dest. water		10	0.2	CA 50	0.35	0.13	0.66	0.7
						0.38	3.7	4
						0.31	2.7	2.9
						0.22	1.5	1.7
						0.13	0.6	0.75
0.1M Na-citrate 4	4	9.6	0.2	CA 50	0.37	0.09	0.25	0.35
						0.16	0.75	0.75
						0.40	3.5	3.9
						0.34	2.5	2.8
						0.25	1.7	1.9

Table D-5 (Continued)

Solvent	pH	Amount of solute (mg)	Concentration of solute (g/l)	Membrane type	Membrane resistance	Specific "gel" resistance	Compressive pressure (bar)	Applied pressure (bar)
1M NaCl		8	0.2	CA 50	0.42	0.17	0.75	0.75
						0.45	3.7	4.1
						0.42	2.45	2.35
						0.34	1.4	1.6
						0.29	1.3	1.55
0.1M Na- citrate/HCl	4	9	0.2	CA 50	0.38	0.20	0.55	0.55
						0.2	0.75	0.75
						0.38	2.7	3
						0.29	1.55	1.8
						0.18	0.65	0.75
0.15M NaCl		9.4	0.2	CA 50	0.33	0.51	3.85	4.1
						0.41	2.8	3
						0.33	1.85	2
						0.23	0.8	0.9
						0.23	0.9	0.9
0.15M NaCl		9.6	0.2	CA 50	0.39	0.44	4.05	4.3
						0.39	2.9	3.2
						0.30	1.9	2.15
						0.24	1	1.15
0.15M NaCl		10	0.2	CA 50	0.30	0.49	4	4
0.15M NaCl		8	0.17	CA 50	0.32	0.44	4	4

0.15M NaCl	10	0.2	CA 50	0.38	0.47 0.46 0.40 0.32 0.23	4 3.7 2.8 1.9 0.95	4 4 3.1 2.1 1.1
0.2M fosfate	7 47	1	DDS 600	2.4	0.49 0.55 0.33	3 4.3 1.45	3 4.3 1.45
0.2M fosfate	7 47	1	DDS 600	1.30	0.50 0.54 0.35	3 4.3 1.45	3 4.3 1.45
0.15M NaCl	2.6 49	1	CA 50	0.36	0.47 0.53 0.41 0.31 0.23	2.65 4.3 2.6 1.5 0.8	2.65 4.3 2.6 1.5 0.8
0.15M NaCl	10	0.1	CA 50	0.36	0.12	0.83	1.25

Appendix E: The significance of measured diffusion coefficients.

The diffusion coefficients reported in literature are often measured by methods that are readily described by the diffusion coefficient designated D_A^V by Hartley and Crank, that is the coefficient defined

$$N_A = D_A^V \frac{dc_A}{dx} \quad (E-1)$$

Flux of a solute = D_A^V concentration gradient of the solute where the flux is measured across a plane through which no volumetric flow occurs in isothermic isobaric binary system.

To find the relationship between D_A^V and other diffusion coefficients, let us consider a typical diffusion experiment. The generalized Stefan-Maxwell equation for a species i (from Scattergood and Lightfoot, 1968)

$$\begin{aligned} -RTV \ln a_i + M_i \left(g_i - \sum_{j=1}^n \omega_j g_j \right) - (\bar{V}_i - 1/c_i) \nabla p = \\ = \sum_{j=1}^n (RT/D_{ij}c_i)(X_jN_i - X_iN_j). \end{aligned} \quad (E-2)$$

Here the a_i represent thermodynamic activities of the species i , calculated for local chemical composition but with reference temperature and pressure; the X_i , ω_i , and c_i are species mole fractions, mass fractions, and molar concentrations; M_i species molecular weights; $\bar{V}_i$ partial molal volumes, and the N_i molar fluxes (moles/area time) relative stationary co-ordinates. The g_i are total body forces per unit mass acting on the species i . The D_{ij} are generalizations of the Stefan-Maxwell diffusivities and have the symmetry property $D_{ij} = D_{ji}$.

For binary solution unaffected by body forces (no electrical or magnetic fields, gravitational field disregarded), without pressure gradient and one-dimensional, and assuming constant partial molar volumes,

$$-RT \frac{d \ln a_A}{dx} = \frac{RT}{D_{AB} c_A} (X_B N_A - X_A N_B) \quad (E-3)$$

The condition of no volumetric flow is

$$\bar{V}_A N_A + \bar{V}_B N_B = 0 \quad (E-4)$$

Substituting

$$X_A = \frac{c_A}{c_A + c_B}, \quad X_B = 1 - X_A, \quad \phi_A = \bar{V}_A c_A,$$

$$\frac{d \ln a_A}{dx} = \frac{\delta \ln a_A}{\delta \ln c_A} \cdot \frac{1}{c_A} \frac{dc_A}{dx} \quad (E-5)$$

one arrives at

$$\left(\frac{c_A}{c_B} + 1 \right) \phi_B \frac{\delta \ln a_A}{\delta \ln c_A} D_{AB} \frac{dc_A}{dx} = N_A \quad (E-6)$$

Comparing Eq E-1 and Eq. E-6 gives

$$D_A^v = D_{AB} \frac{\delta \ln a_A}{\delta \ln c_A} \phi_B \left(\frac{c_A}{c_B} + 1 \right) \quad (E-7)$$

For protein solutions of any concentration, the last term of Eq. E-7 may be dropped safely in view of the enormous difference of molecular weights.

